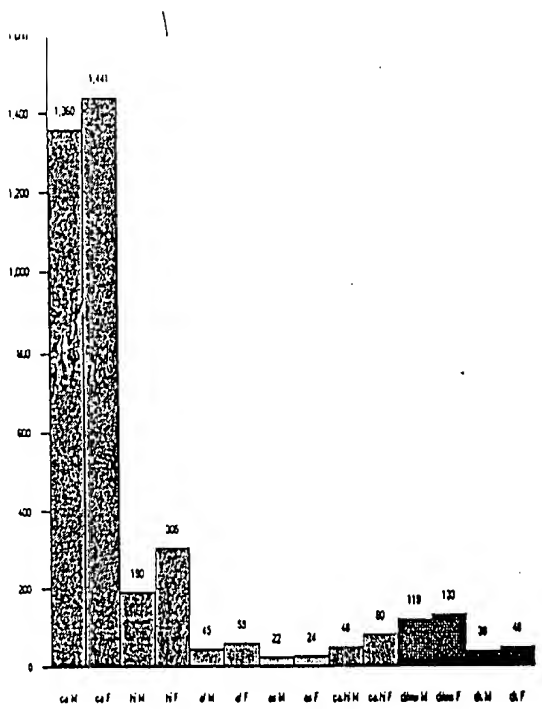
DOETOT:E8H28960

Sample Bank

SEQUENOM
INDUSTRIAL GENOMICS

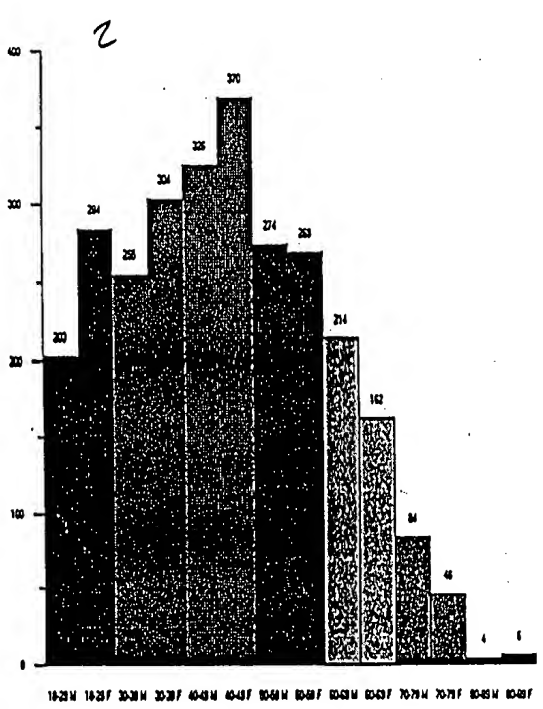
DNA Bank

Number of Samples: 3912



Caucasians

Number of Samples: 2901



Hispanics

Number of Samples: 495

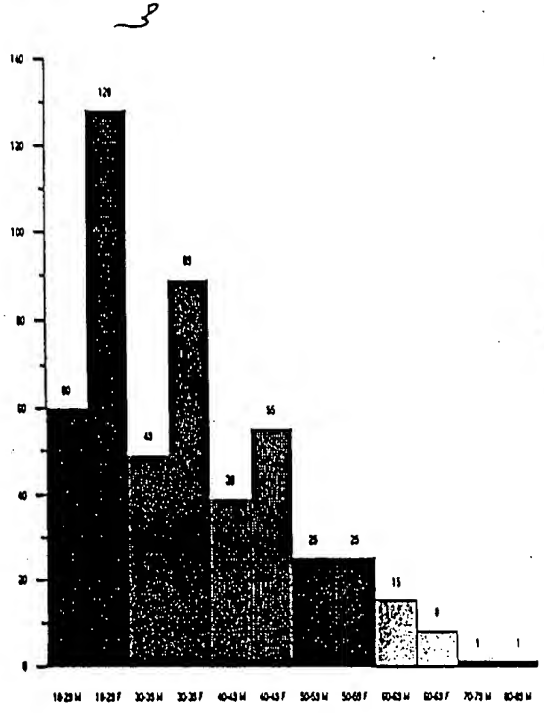
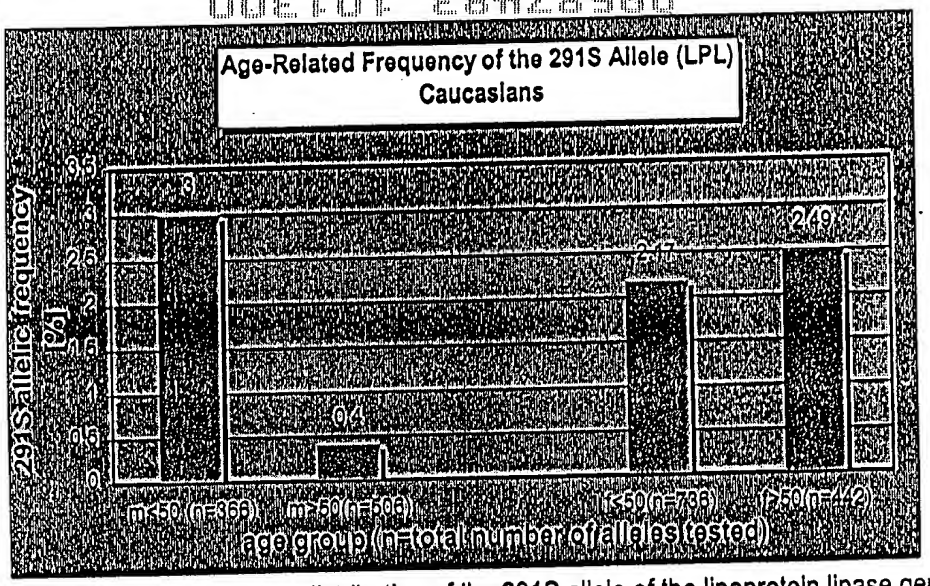


FIGURE 1

DOCTOR "EP1278960

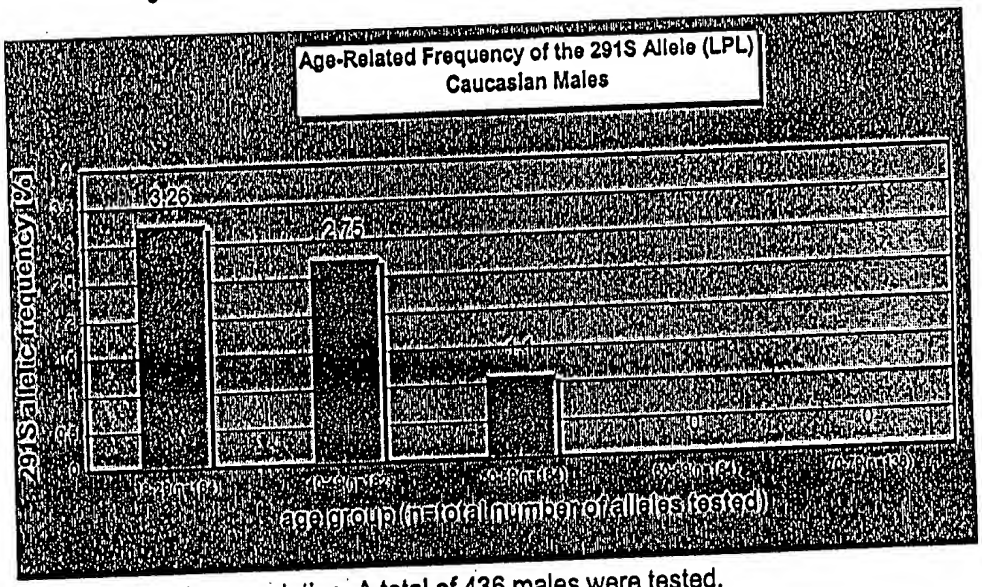
FIGURE 2A



age- and sex-distribution of the 291S allele of the lipoprotein lipase gene. A total of 436 males and 589 females were investigated.

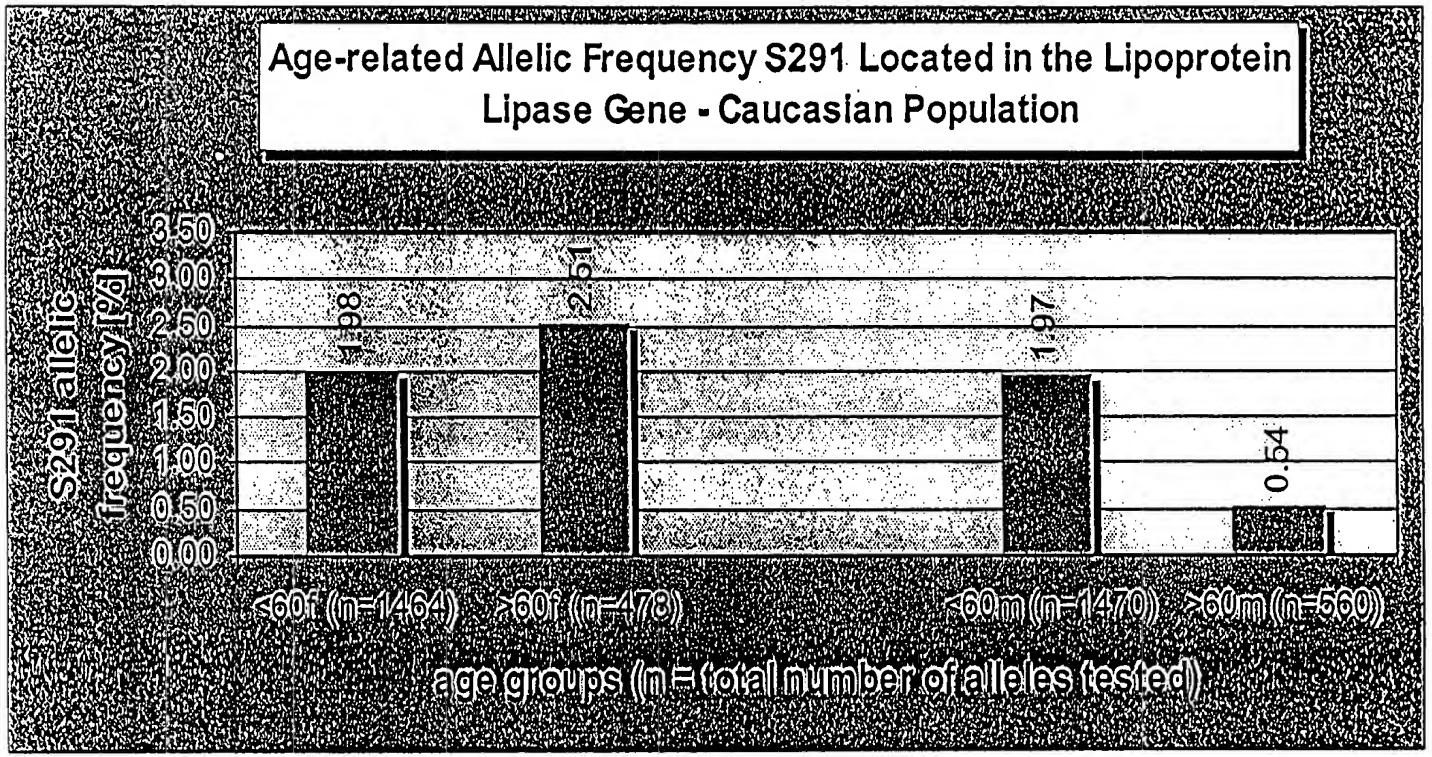
FIGURE 2B

Age-related distribution of the 291S allele of the lipoprotein lipase gene within the



male Caucasian population. A total of 436 males were tested.

09E70T "E8h78960



Significance: Allele frequency of Ser291drops from 1.97% to 0.54% in males; p=0.009

FIGURE 2C

00EFOT"E8h78960

Intelligent Genomics

SEQUENOM
INDUSTRIAL GENOMICS

Questionnaire for Population-Based Sample Banking

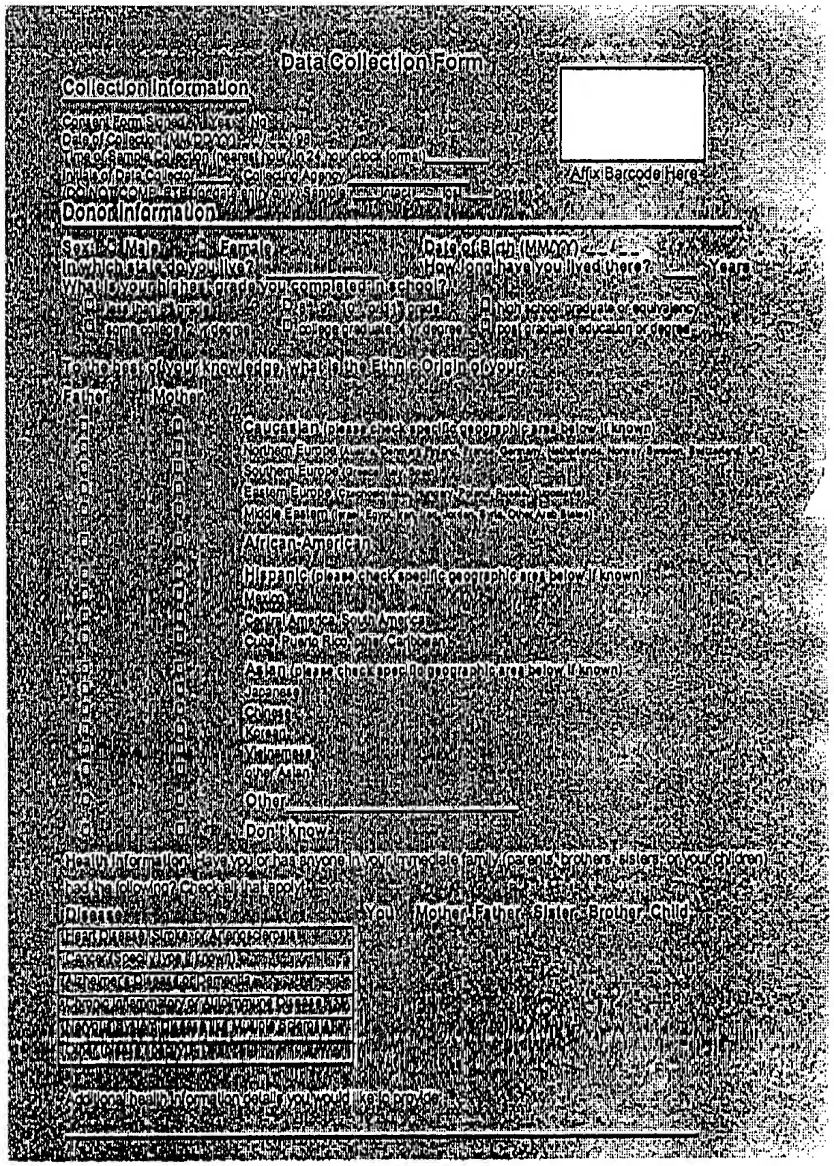


FIGURE 3

00E10T"E8h28960

Intelligent Genomics

SEQUENOM
INDUSTRIAL GENOMICS

Sample Banks

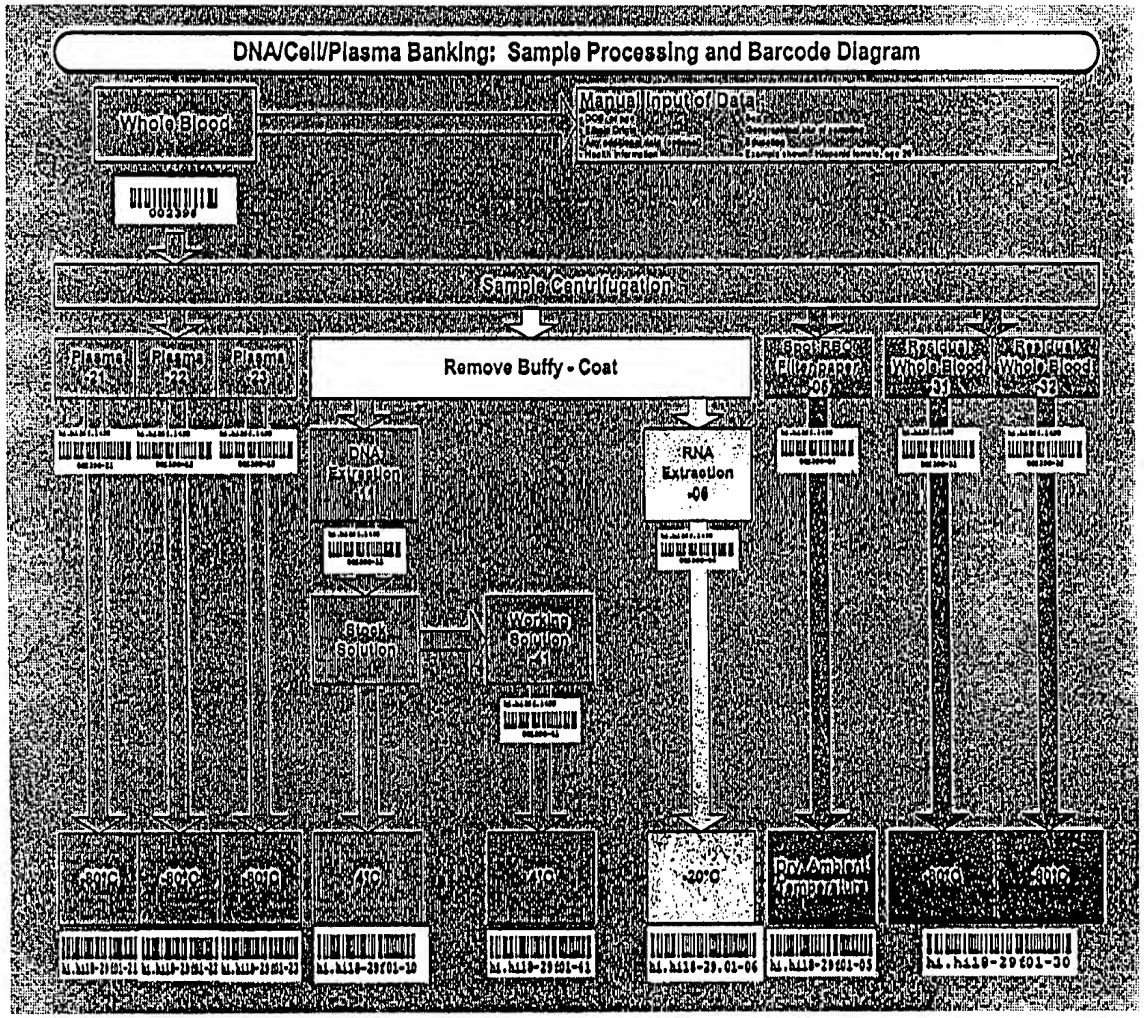


FIGURE 4

00E70T"E8h78960

Intelligent Genomics

SEQUENOM
INDUSTRIAL GENOMICS

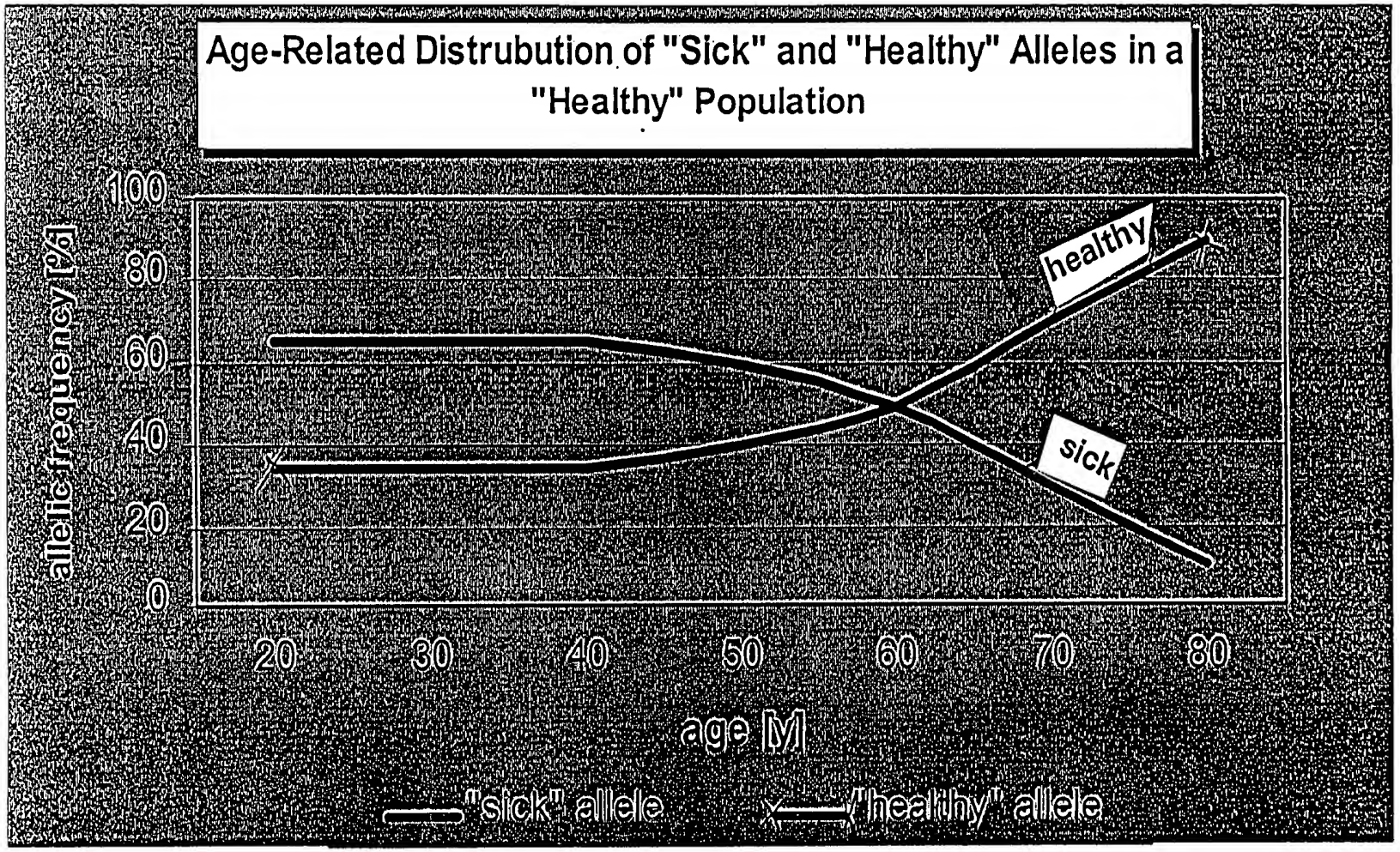


FIGURE 5

DOETOT"E8h78960

Intelligent Genomics

SEQUENOM
INDUSTRIAL GENOMICS

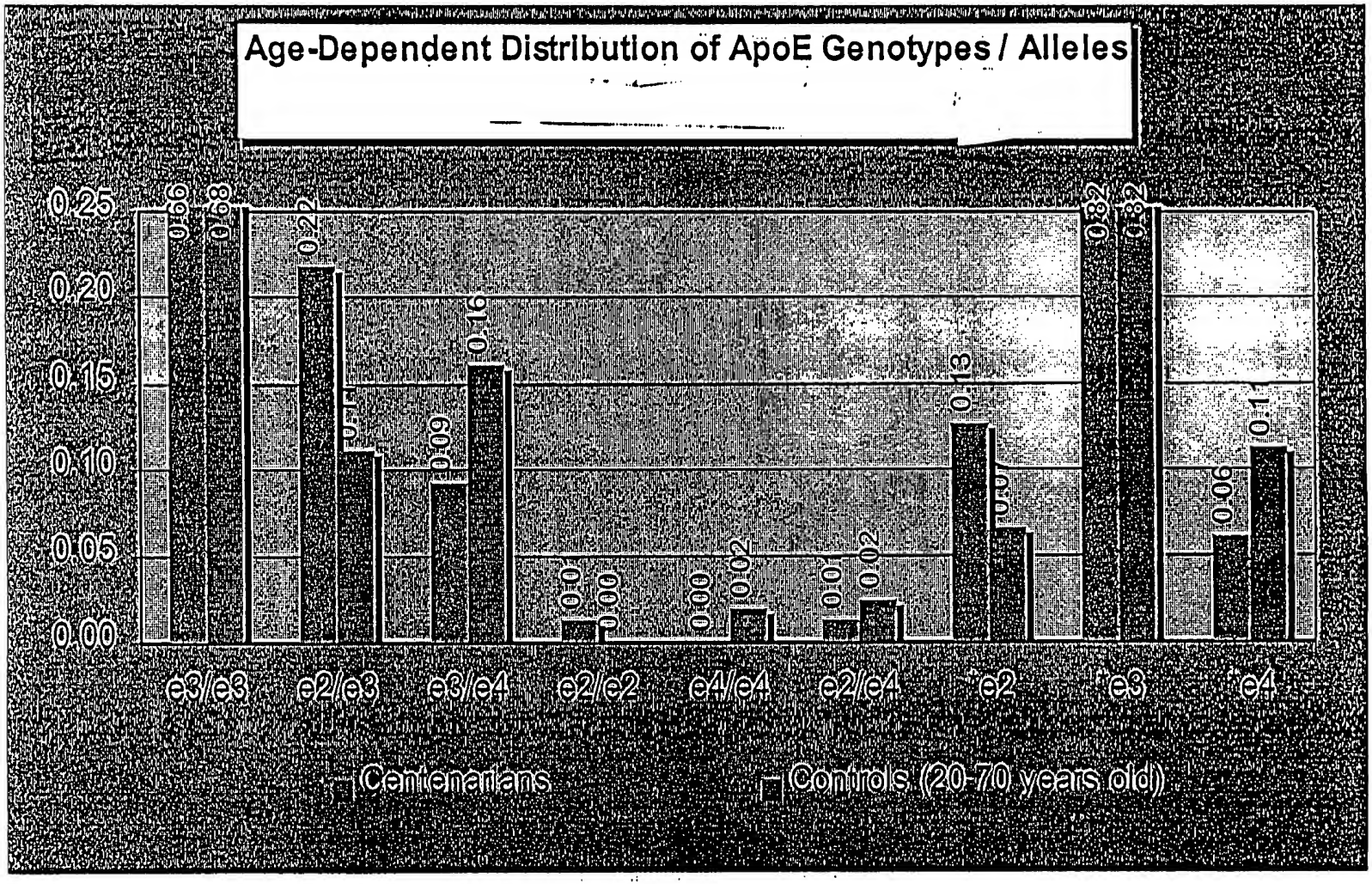


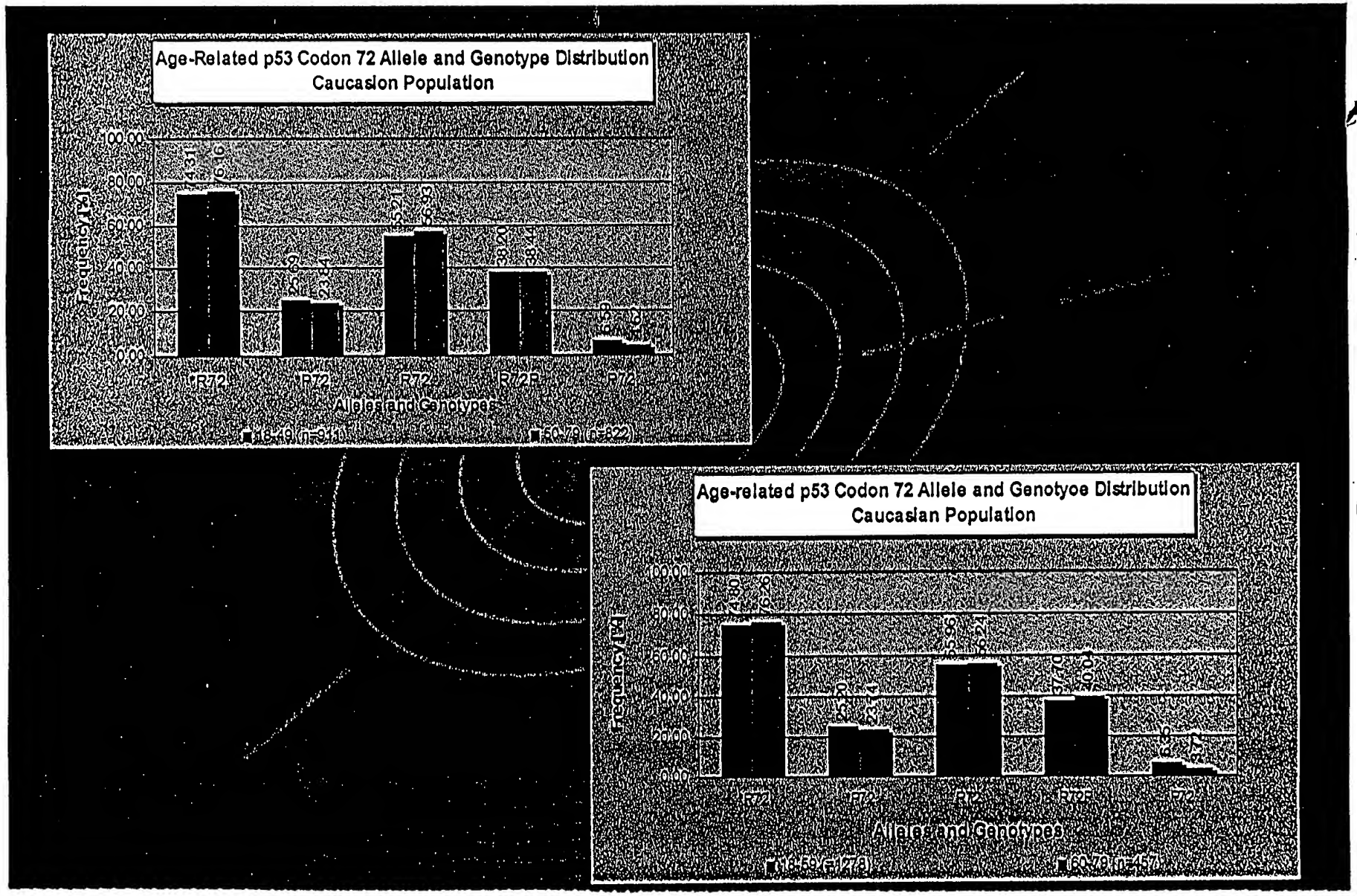
FIGURE 6

DOETOF"E8h78960

FIGURE 7A

SEQUENOM
INDUSTRIAL GENOMICS

i genetics



DOETOT"E8h78960

SEQUENOM
INDUSTRIAL GENOMICS

i genetics

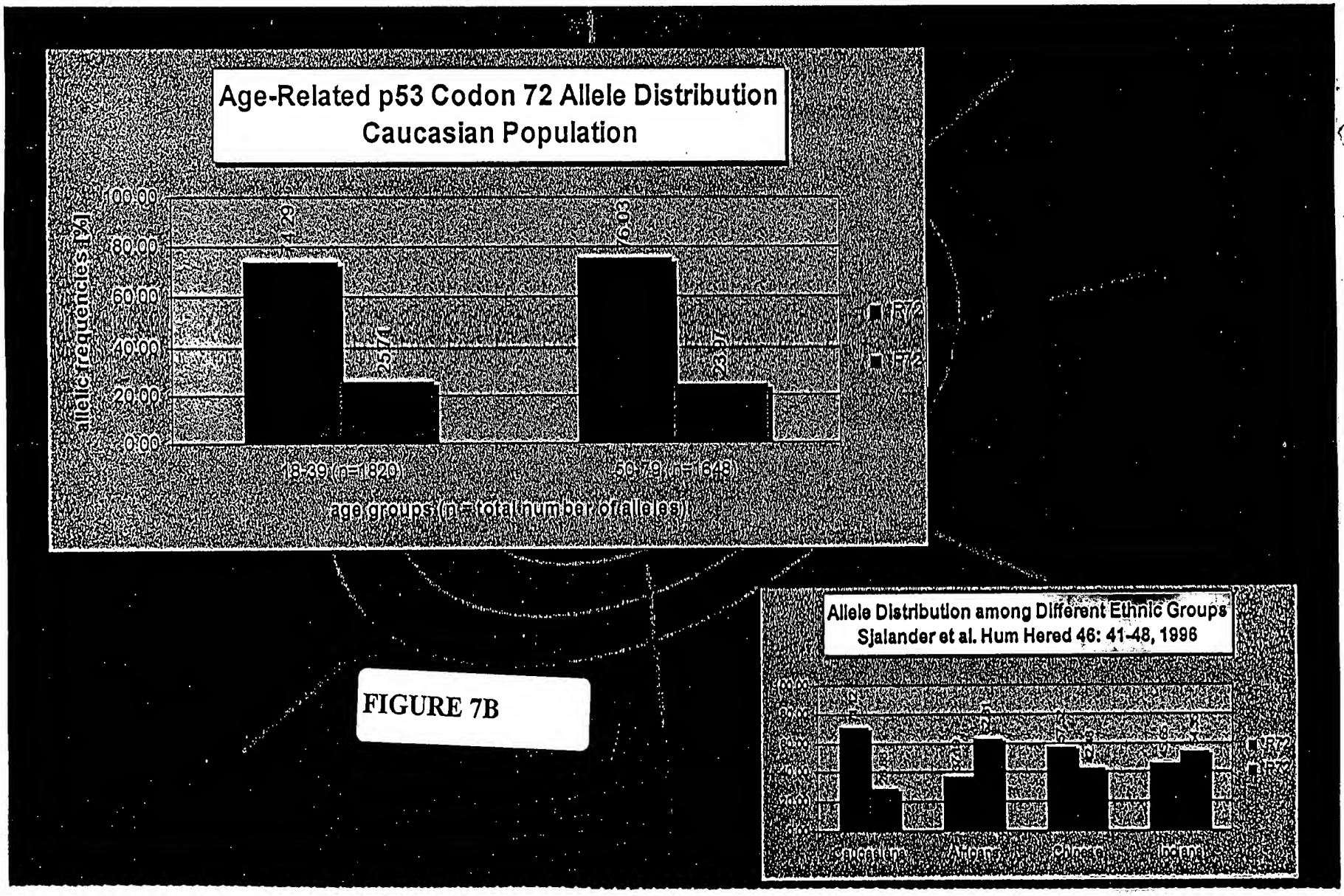


FIGURE 7B

00ETOT'E8h28960

FIGURE 7C

SEQUENOM
INDUSTRIAL GENOMICS

i genetics

P53 PP vs. PR/RR Genotype Distribution By Age cut point = 59

Age Group	N	Genotype Freq (%) PP	PR/RR
18-59	1278	6.7	93.4
60-79	457	3.7	96.3

Sample Size : 1735

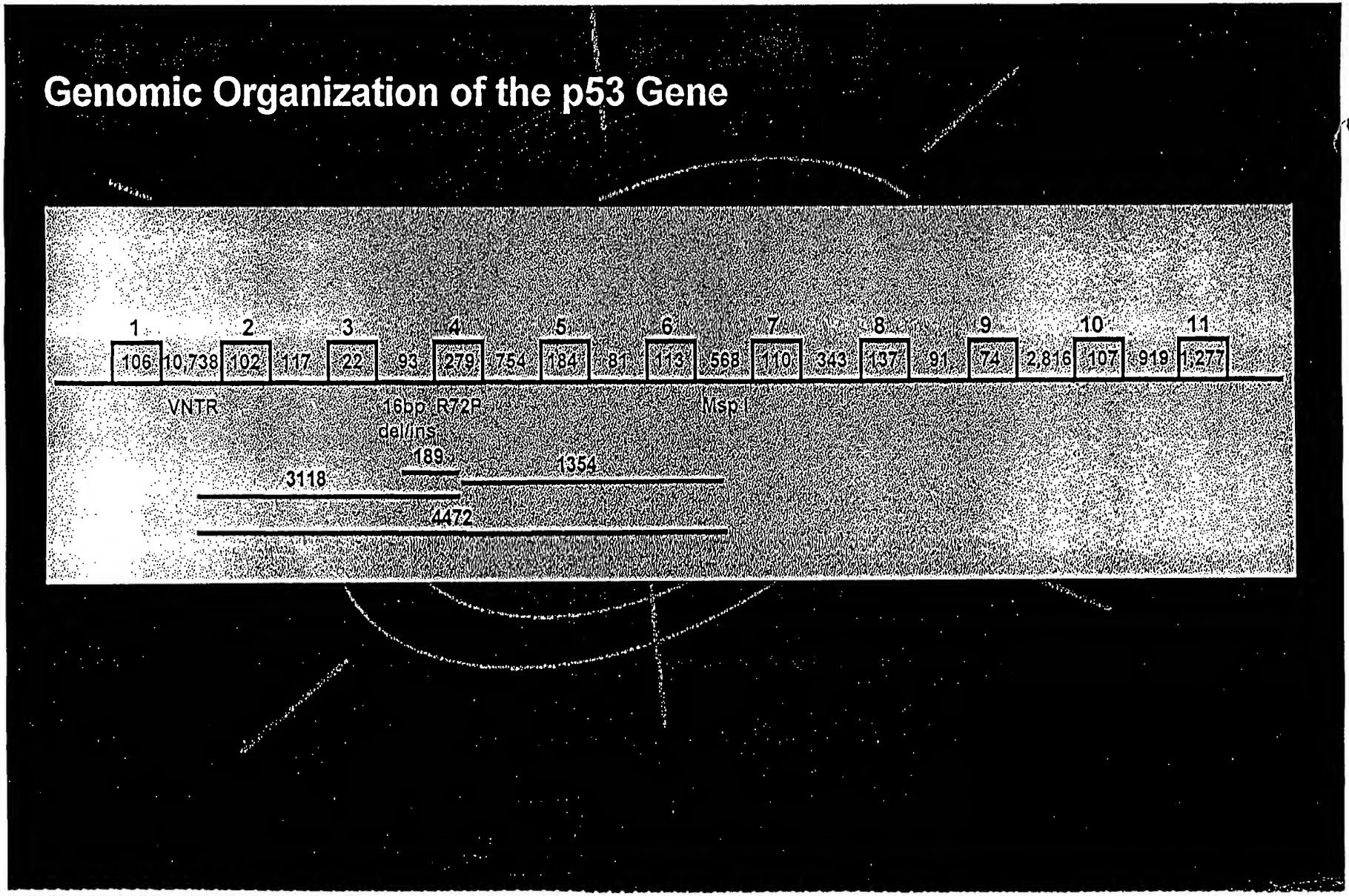
χ^2 : 5.2 (1 d.f.), P = **0.02**

00E70T "E8h28960

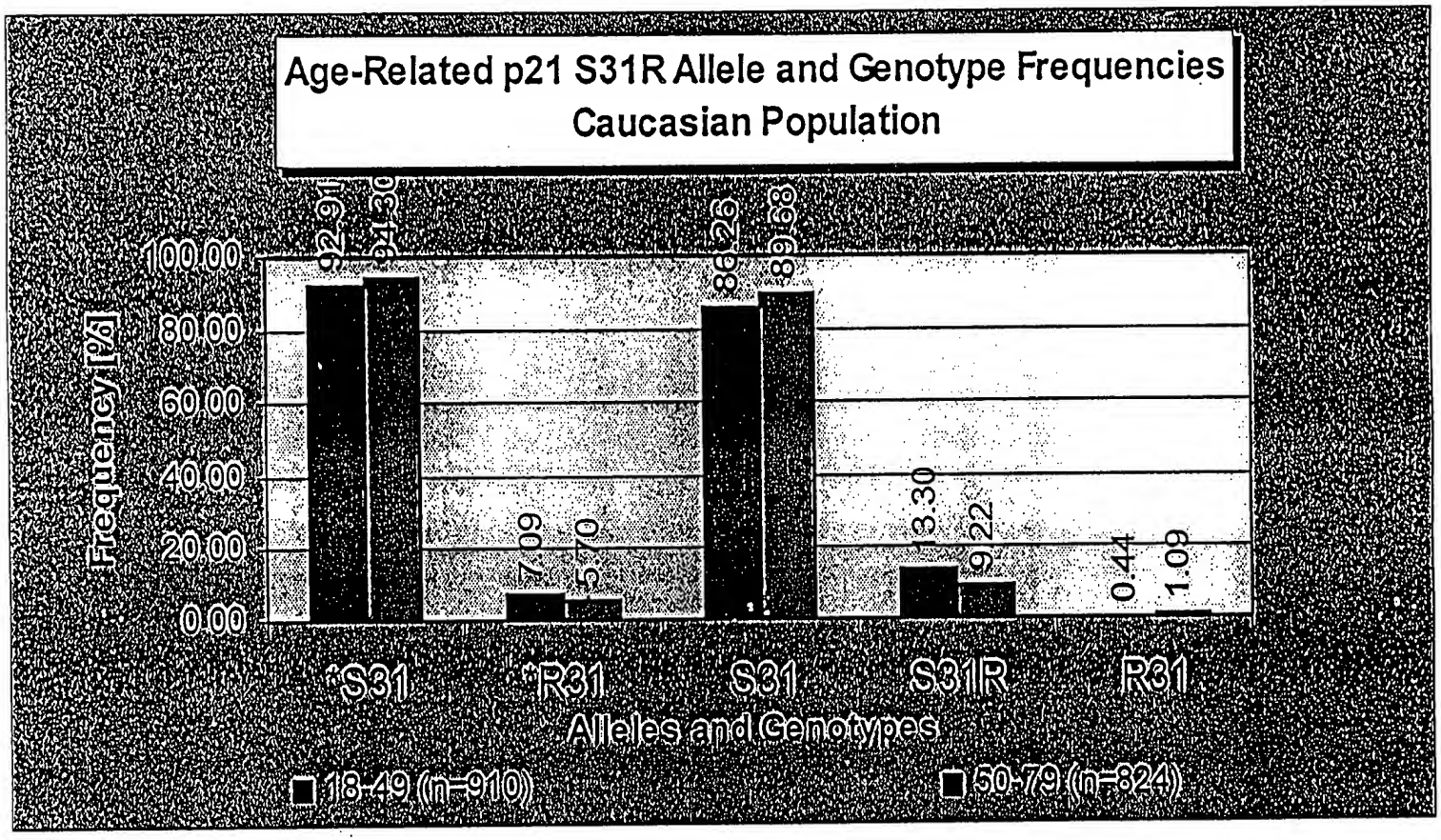
FIGURE 7D

SEQUENOM
INDUSTRIAL GENOMICS

i genomics



00E70T "EBh78960



Significance: Genotype frequency of SR heterozygous drops from 13.3% to 9.2%; p=0.009

FIGURE 8

DOCTOT "EP1428960

DNA MassArray™

FVII R353Q

SEQUENOM
INDUSTRIAL GENOMICS

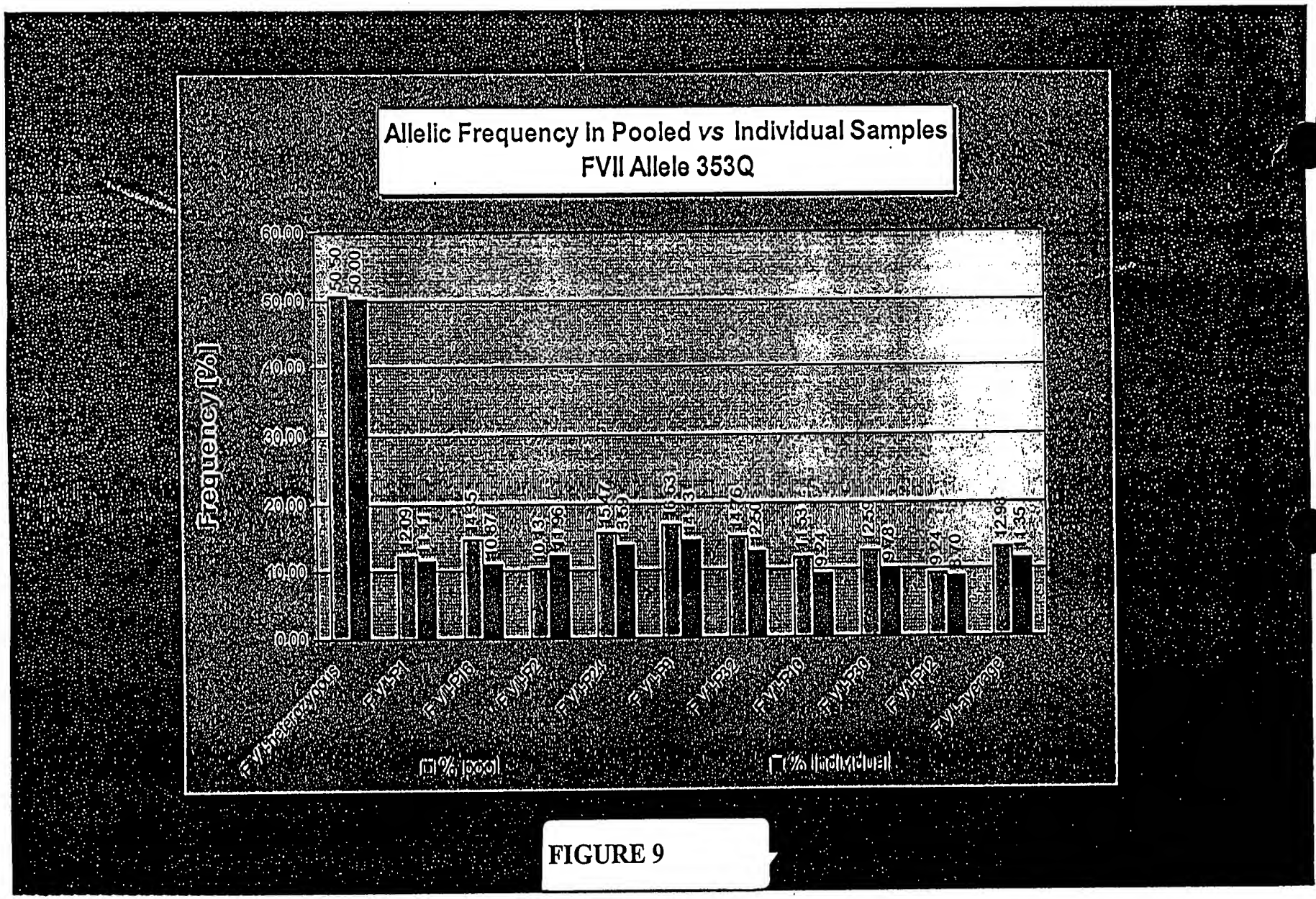


FIGURE 9

00E707 EBH78960

DNA MassArray™

CETP I405V

SEQUENOM
INDUSTRIAL GENOMICS

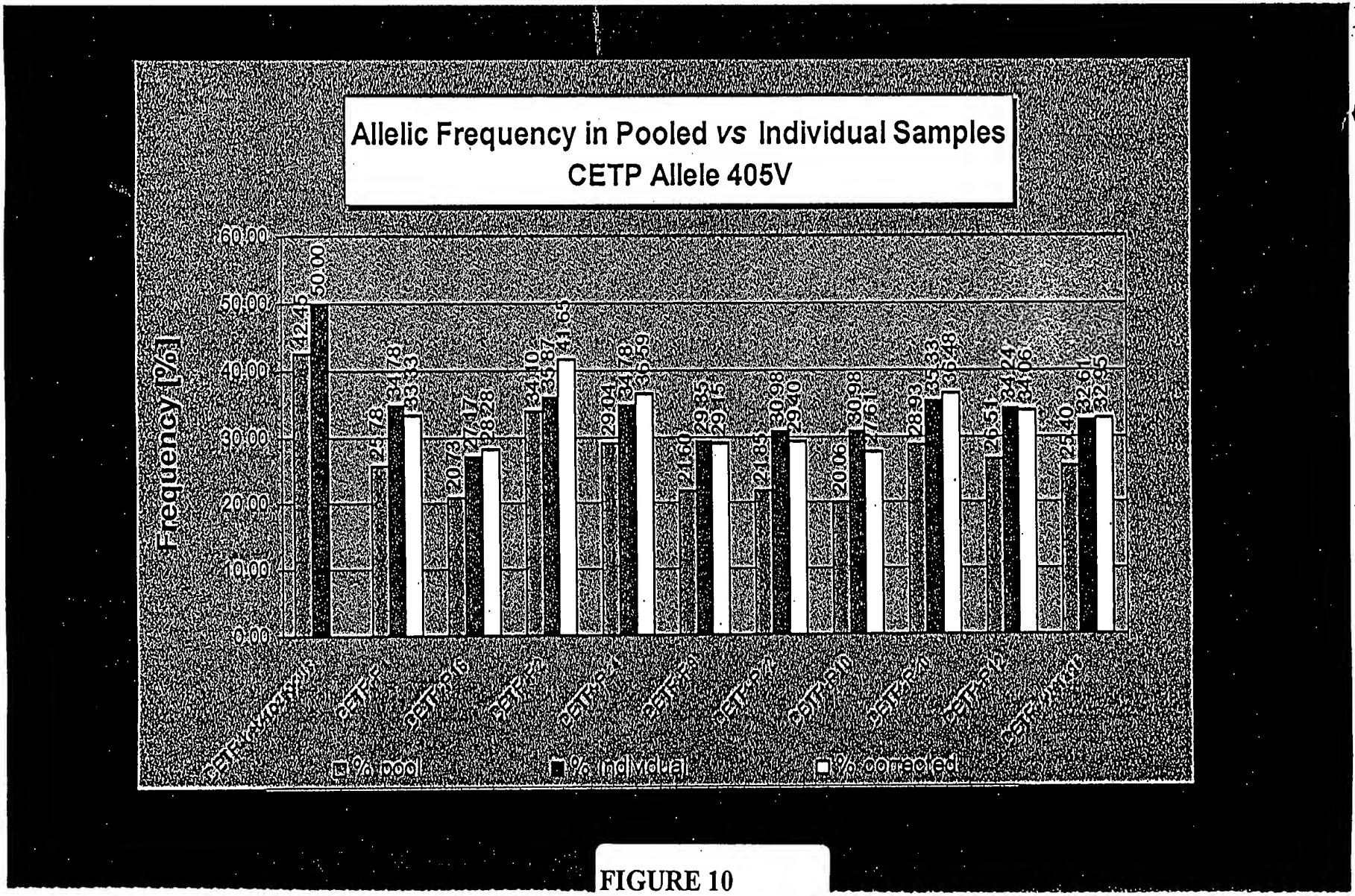


FIGURE 10

00ETOT"E8h78960

DNA MassArray™

PAI-1 4G/5G

SEQUENOM
INDUSTRIAL GENOMICS

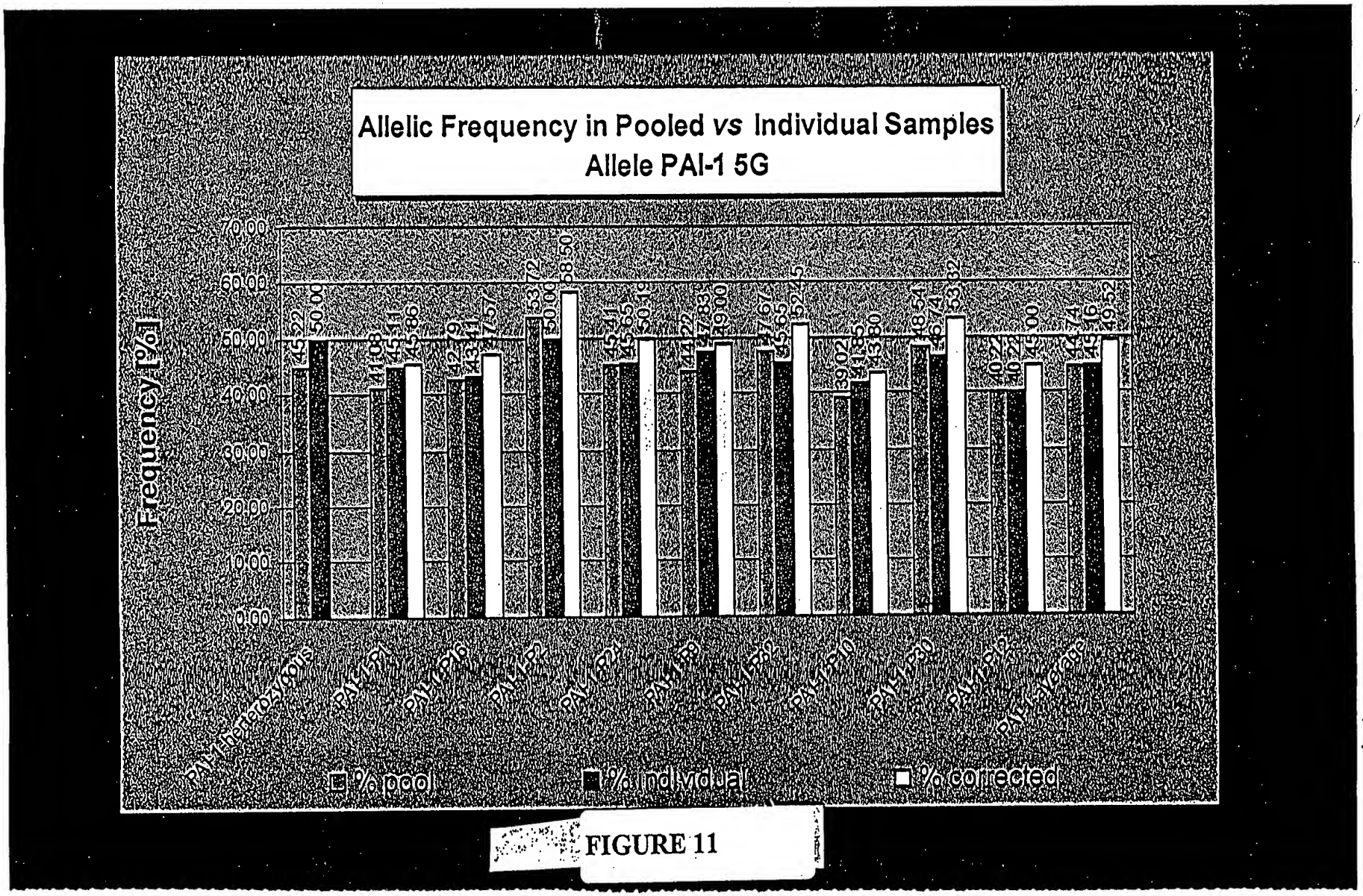


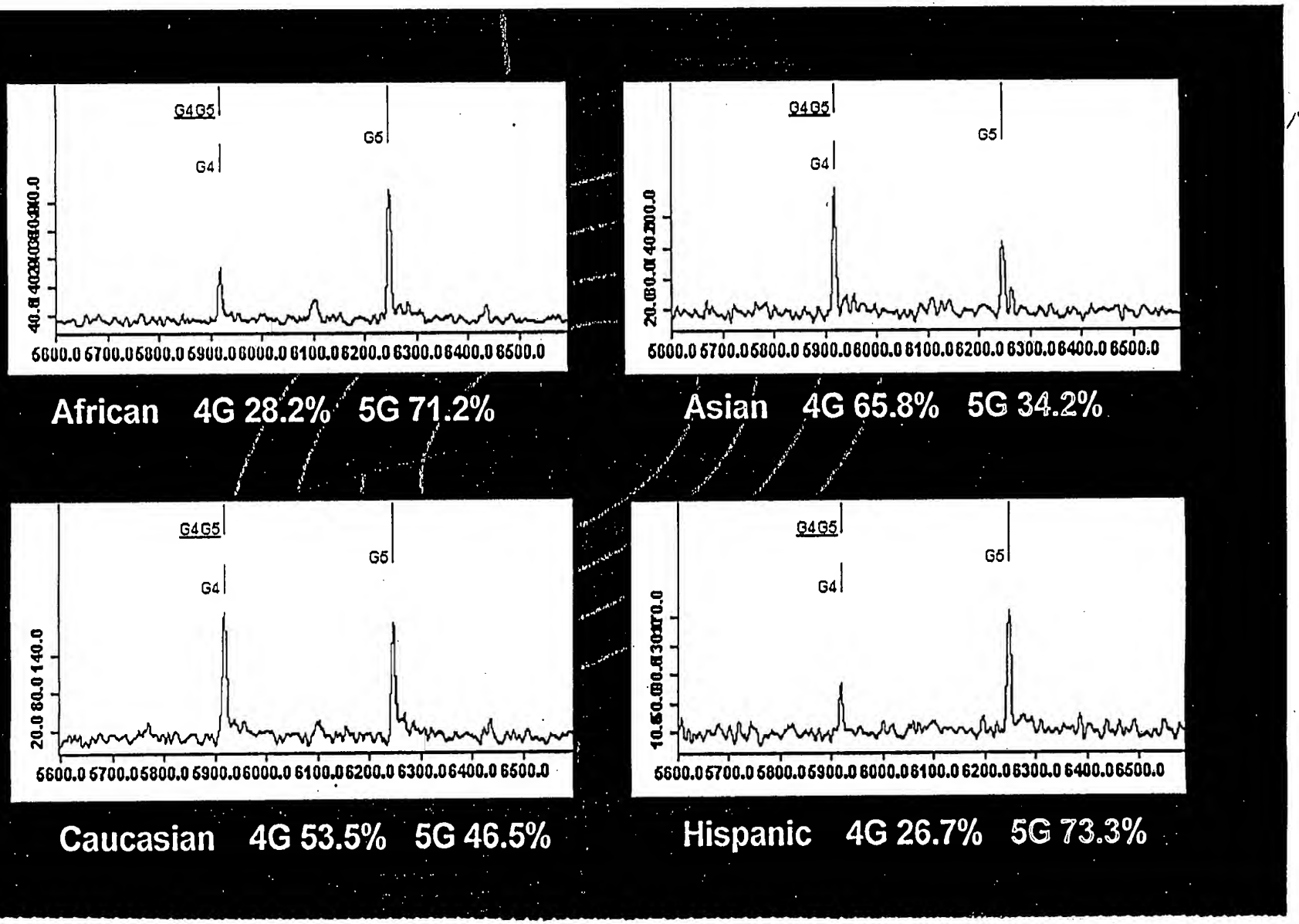
FIGURE 11

DNA MassArray™

Ethnic Diversity (PAI-1)

FIGURE 12

SEQUENOM
INDUSTRIAL GENOMICS

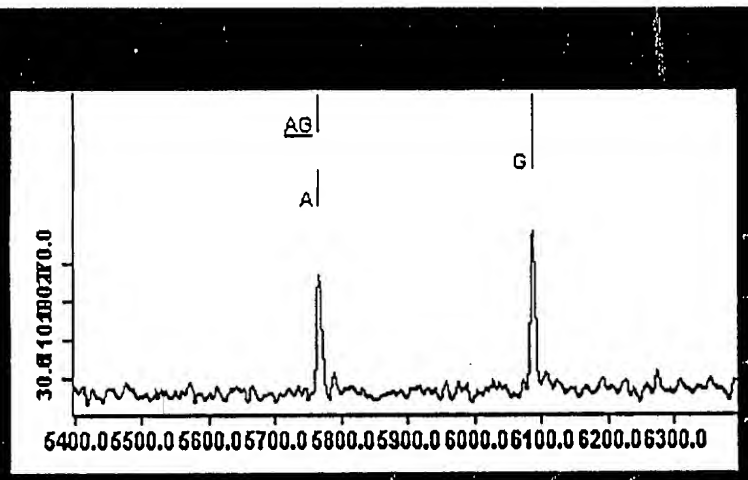


00ETOT"E8h28960

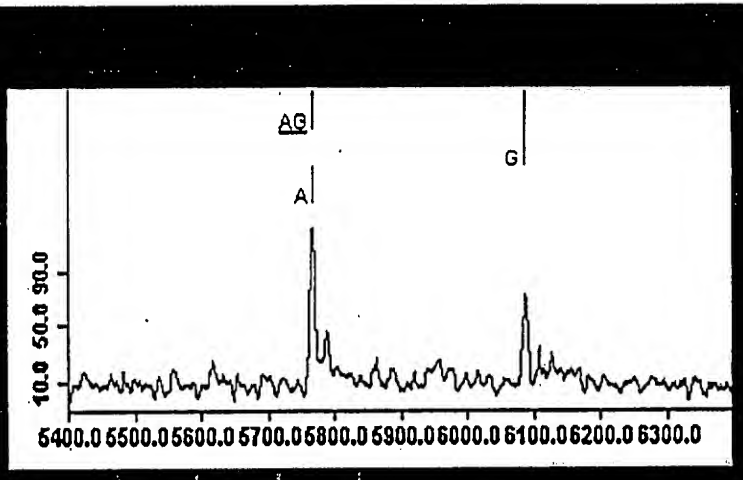
DNA MassArray™

Ethnic Diversity (CETP 405)

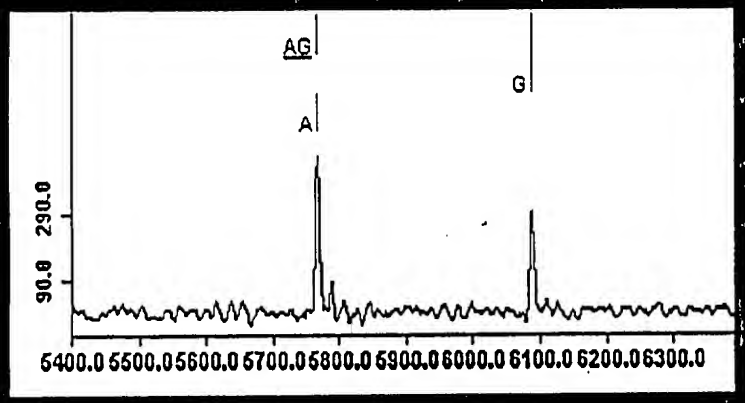
SEQUENOM
INDUSTRIAL GENOMICS



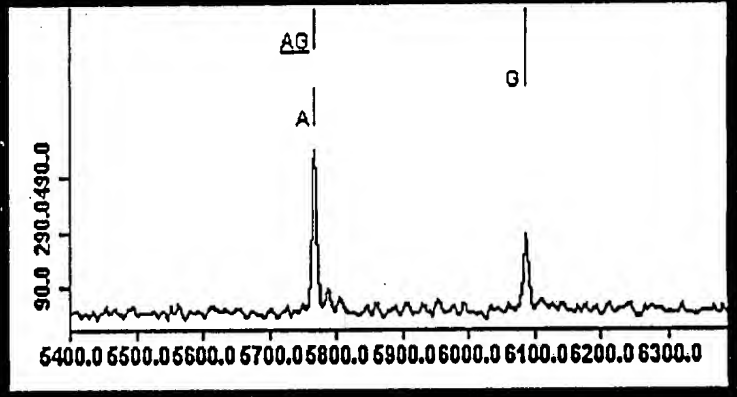
African Ile 43.6% Val 56.4%



Asian Ile 60.7% Val 39.3%



Caucasian Ile 63.0% Val 37.0%



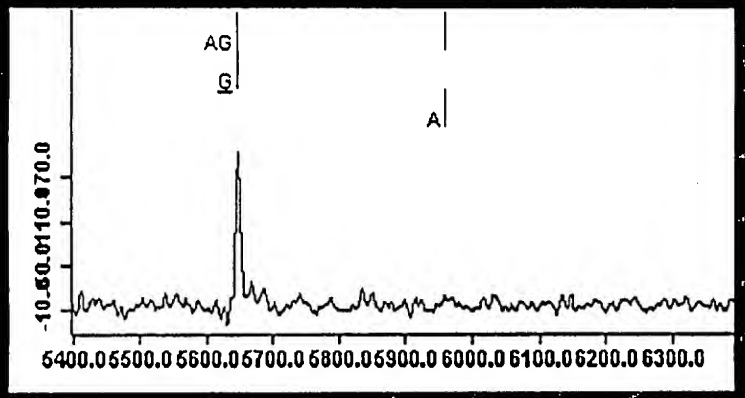
Hispanic Ile 70.1% Val 29.9%

FIGURE 13

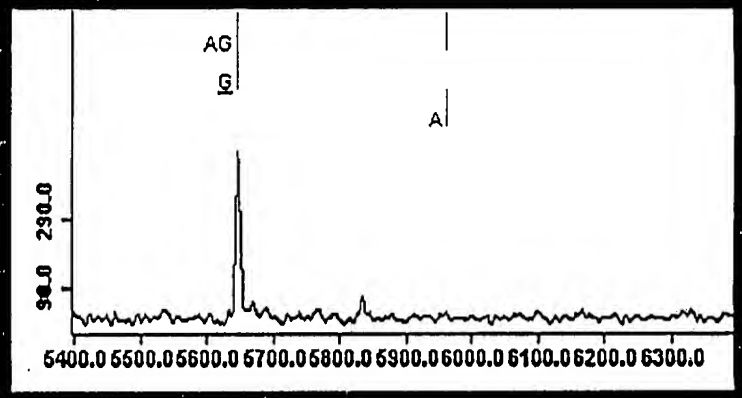
DNA MassArray™

Ethnic Diversity (Factor VII 353)

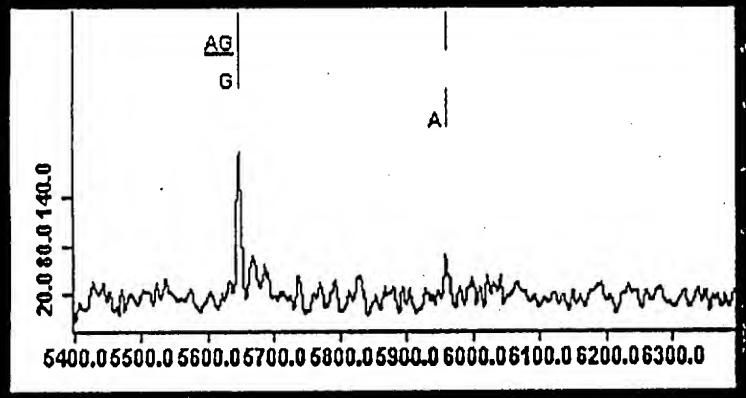
SEQUENOM
INDUSTRIAL GENOMICS



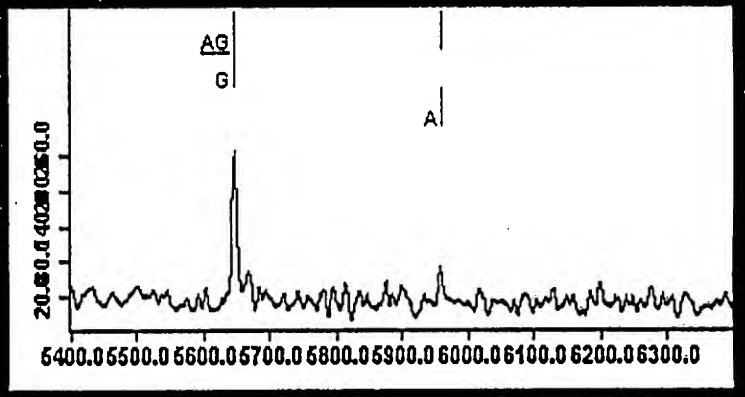
African Arg >95% Glu <5%



Asian Arg >95% Glu <5%



Caucasian Arg 88.5% Glu 11.5%



Hispanic Arg 89.2% Glu 10.8%

FIGURE 14

DNA MassArray™

Ethnic Diversity

SEQUENOM
INDUSTRIAL GENOMICS

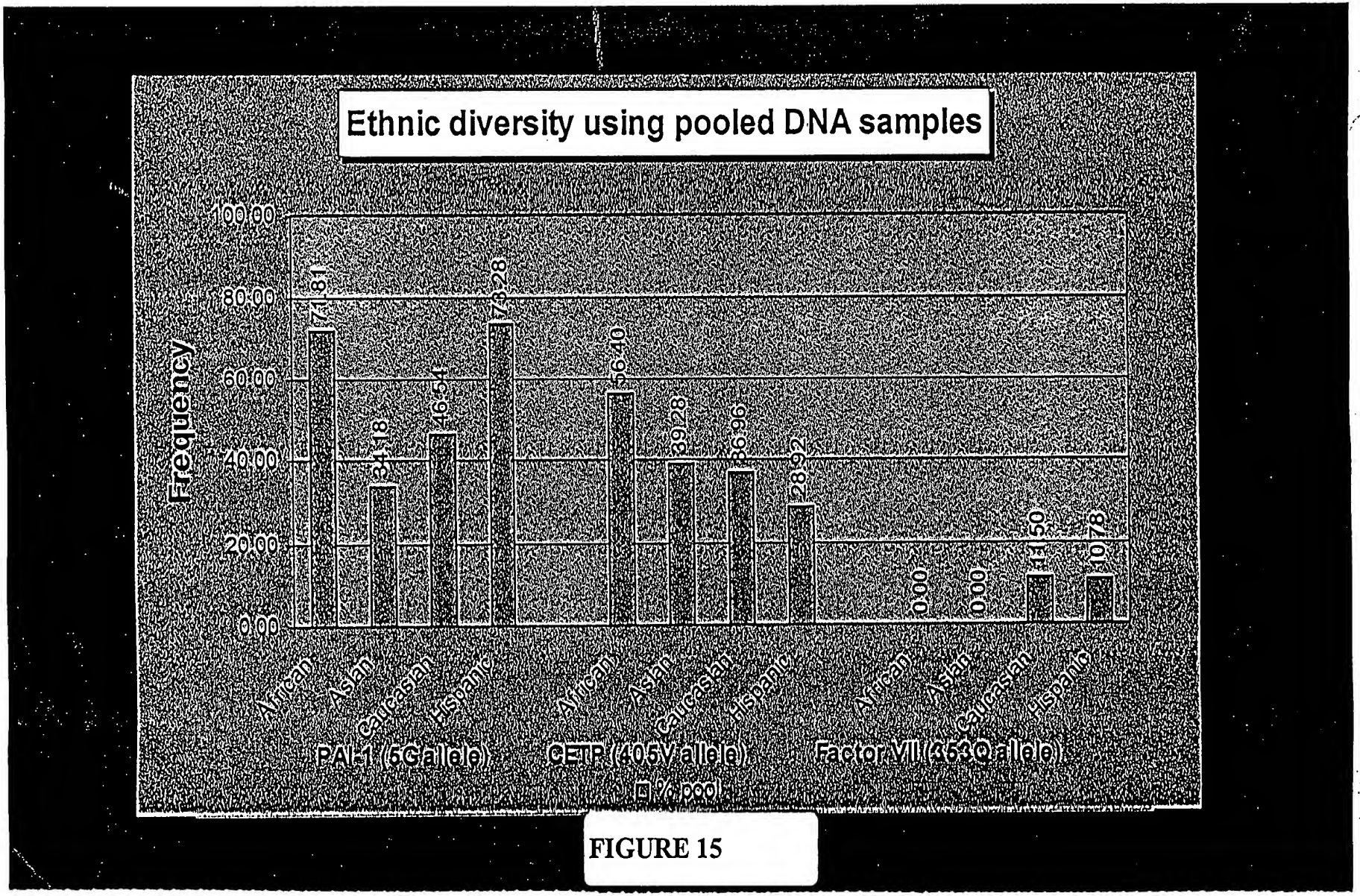
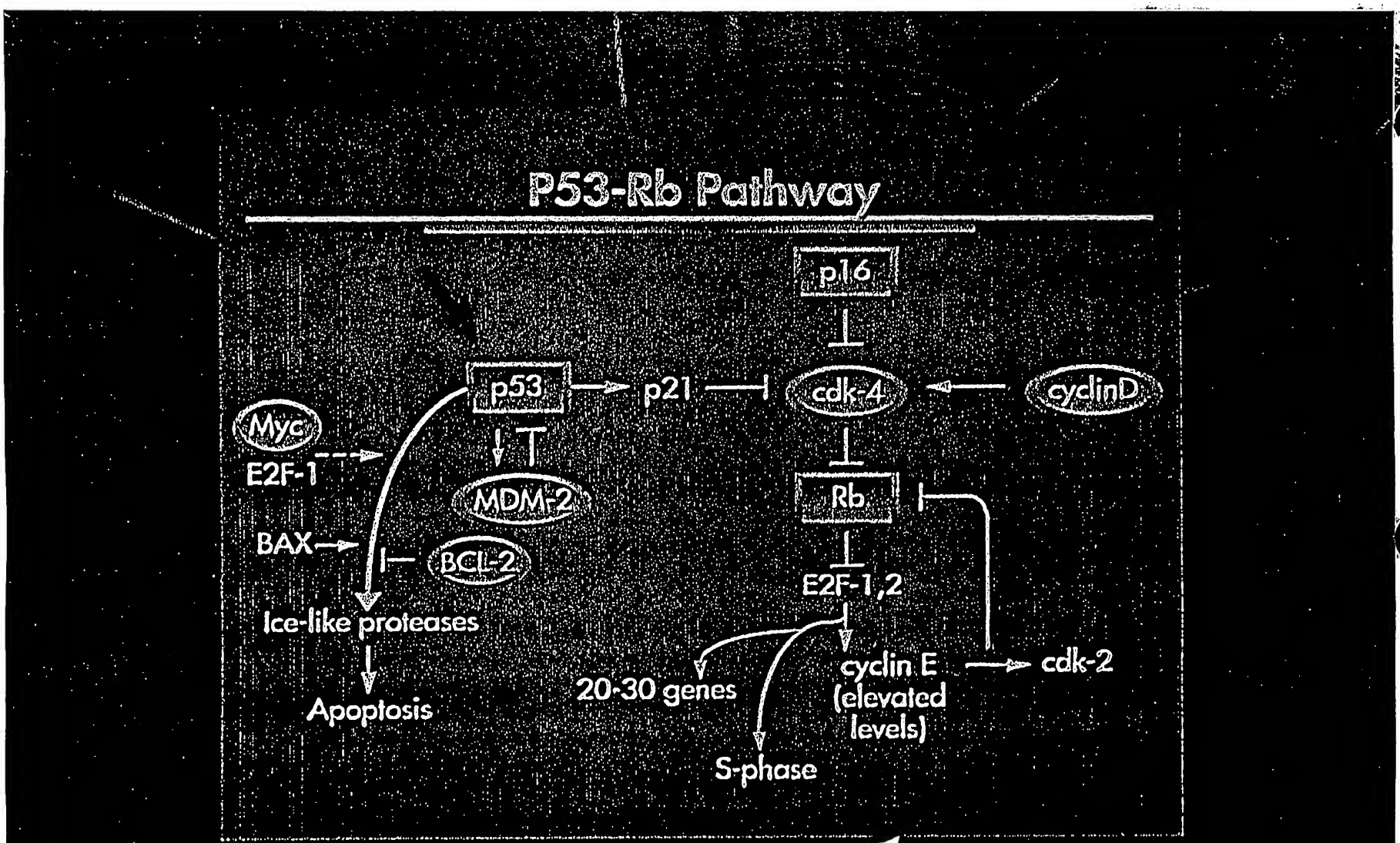


FIGURE 15

SEQUENOM
INDUSTRIAL GENOMICS

i genetics



Levin A. Cell, 88: 323-331, 1997

FIGURE 16

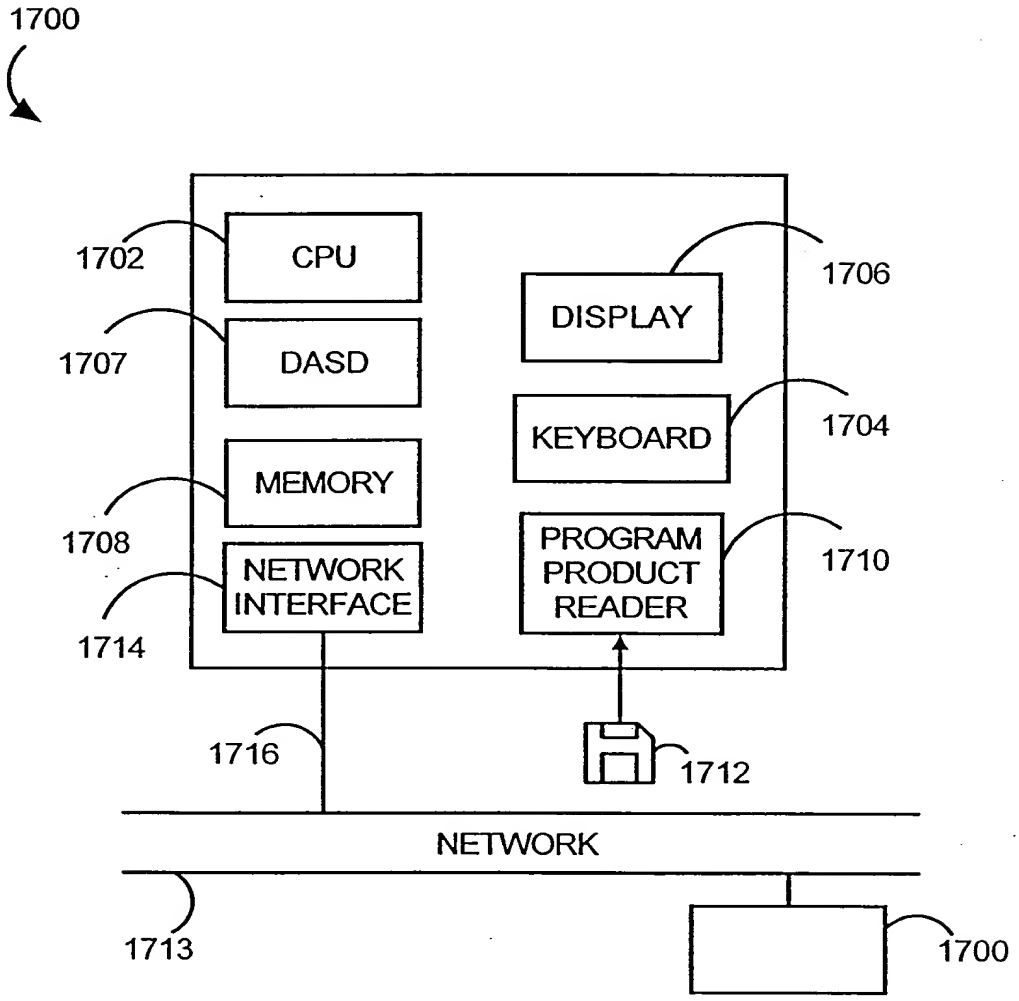

1700
1702
CPU
1706
DISPLAY
1707
DASD
KEYBOARD
1704
MEMORY
1708
PROGRAM
PRODUCT
READER
1710
NETWORK
INTERFACE
1714
1716
1712
NETWORK
1713
1700

FIGURE 17

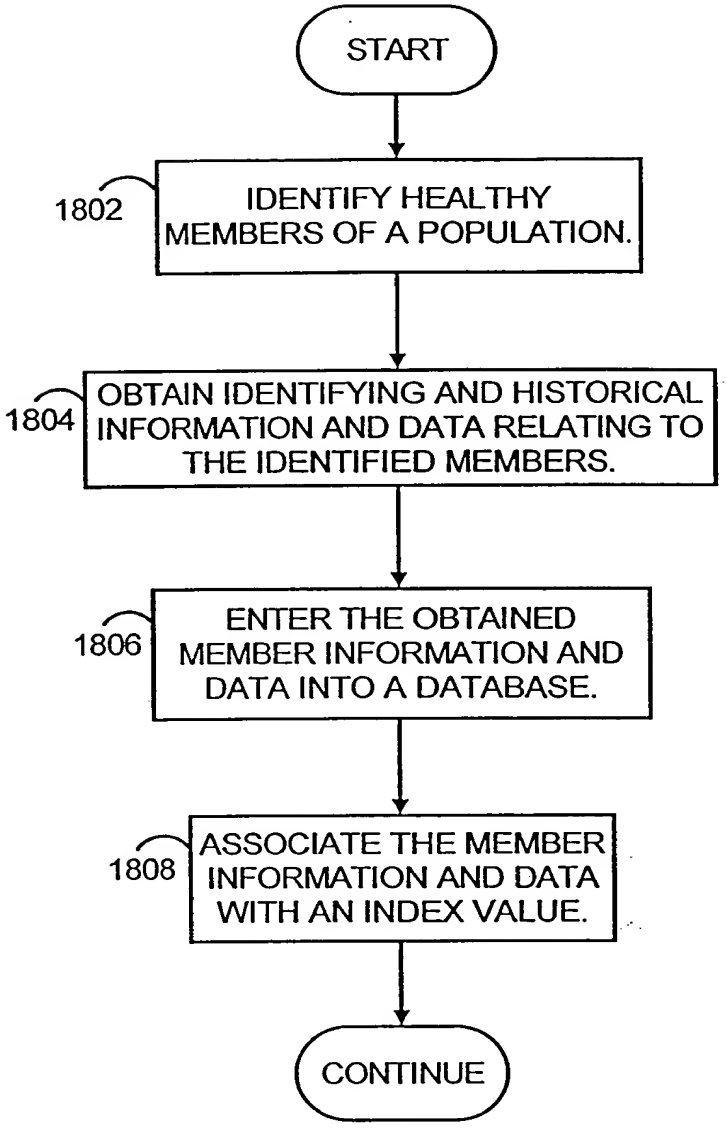

START
1802
IDENTIFY HEALTHY MEMBERS OF A POPULATION.
1804
OBTAIN IDENTIFYING AND HISTORICAL INFORMATION AND DATA RELATING TO THE IDENTIFIED MEMBERS.
1806
ENTER THE OBTAINED MEMBER INFORMATION AND DATA INTO A DATABASE.
1808
ASSOCIATE THE MEMBER INFORMATION AND DATA WITH AN INDEX VALUE.
CONTINUE

FIGURE 18

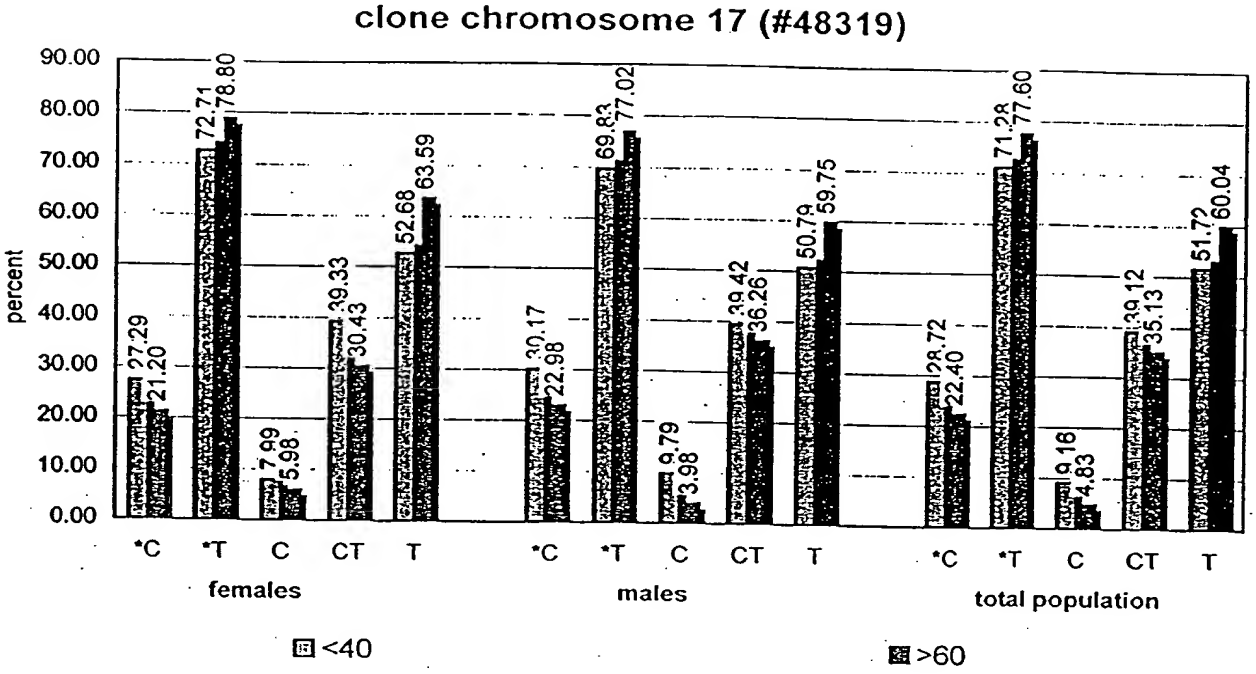


Figure 19

DOCKET: 60h/28950

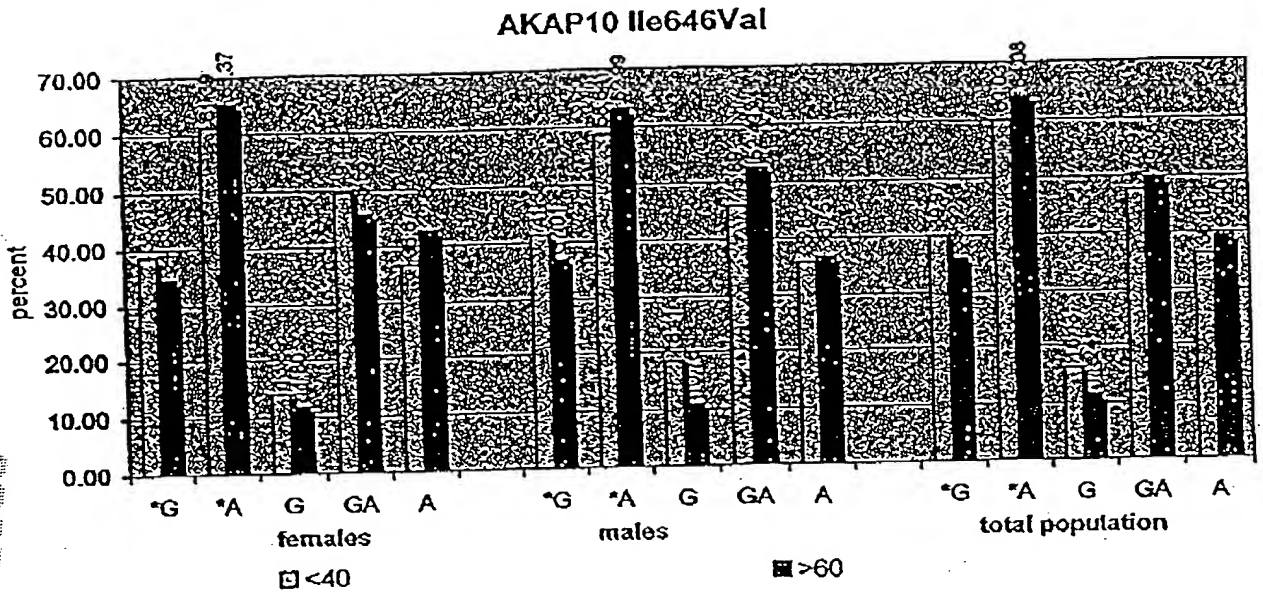
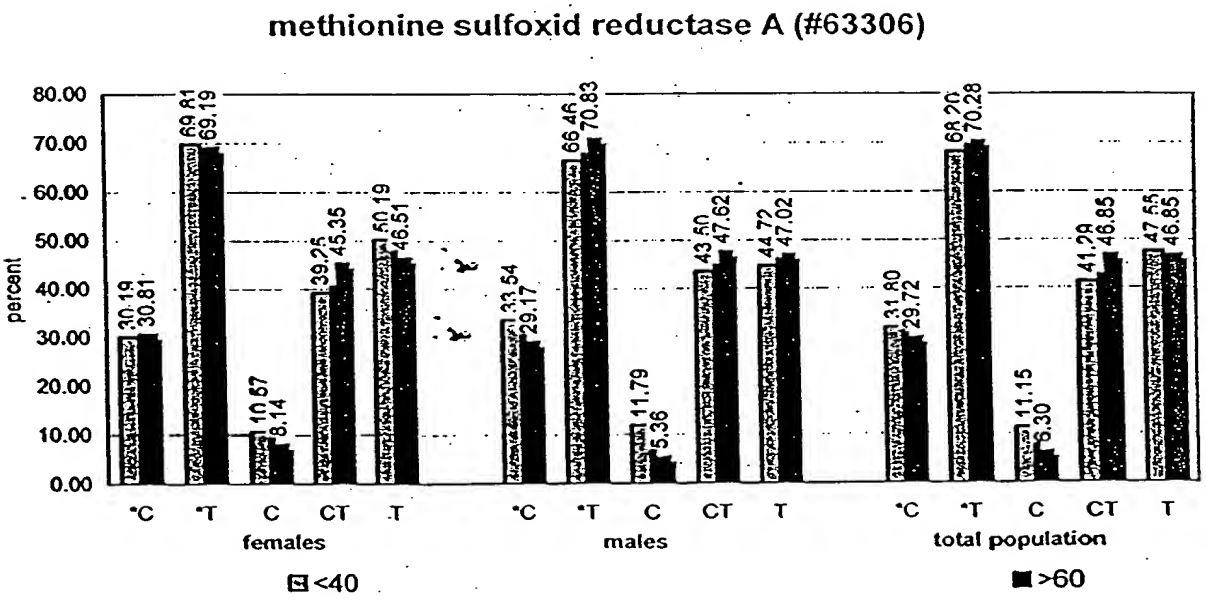


Figure 20

09/834,703 - 2001-04-13

Figure 21


methionine sulfoxid reductase A (#63306)
percent
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
30.19
30.81
69.81
69.19
10.67
8.14
39.25
45.35
50.19
46.51
33.54
29.17
66.46
70.83
11.79
5.36
43.50
47.62
44.72
47.02
31.80
29.72
68.20
70.28
11.15
6.30
41.29
46.85
47.55
46.85
*C
*T
C
CT
T
females
males
total population
<40
>60

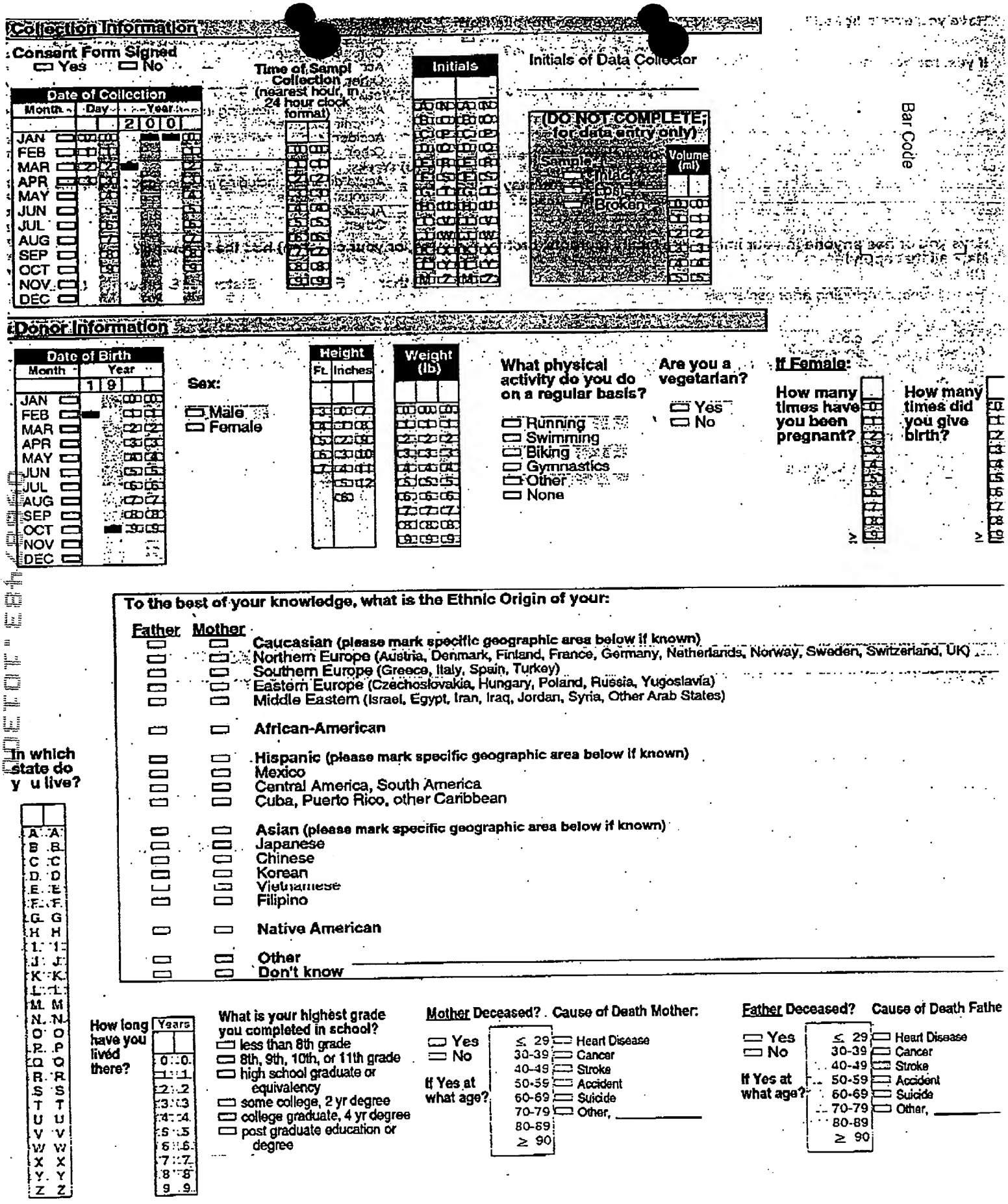

Collection Information
Consent Form Signed
Yes
No
Time of Sampl Collection (nearest hour, in 24 hour clock format)
Initials
Initials of Data Collector
Date of Collection
Month
Day
Year
2 0 0
JAN
FEB
MAR
APR
MAY
JUN
JUL
AUG
SEP
OCT
NOV
DEC
(DO NOT COMPLETE; for data entry only)
Sample
Volume (ml)
Broken
Bar Code
Donor Information
Date of Birth
Month
Year
1 9
Sex:
Male
Female
Height
Ft.
Inches
Weight (lb)
What physical activity do you do on a regular basis?
Running
Swimming
Biking
Gymnastics
Other
None
Are you a vegetarian?
Yes
No
If Female:
How many times have you been pregnant?
How many times did you give birth?
To the best of your knowledge, what is the Ethnic Origin of your:
Father
Mother
Caucasian (please mark specific geographic area below if known)
Northern Europe (Austria, Denmark, Finland, France, Germany, Netherlands, Norway, Sweden, Switzerland, UK)
Southern Europe (Greece, Italy, Spain, Turkey)
Eastern Europe (Czechoslovakia, Hungary, Poland, Russia, Yugoslavia)
Middle Eastern (Israel, Egypt, Iran, Iraq, Jordan, Syria, Other Arab States)
African-American
Hispanic (please mark specific geographic area below if known)
Mexico
Central America, South America
Cuba, Puerto Rico, other Caribbean
Asian (please mark specific geographic area below if known)
Japanese
Chinese
Korean
Vietnamese
Filipino
Native American
Other
Don't know
In which state do you live?
How long have you lived there?
Years
What is your highest grade you completed in school?
less than 8th grade
8th, 9th, 10th, or 11th grade
high school graduate or equivalency
some college, 2 yr degree
college graduate, 4 yr degree
post graduate education or degree
Mother Deceased?
Yes
No
If Yes at what age?
≤ 29
30-39
40-49
50-59
60-69
70-79
80-89
≥ 90
Cause of Death Mother:
Heart Disease
Cancer
Stroke
Accident
Suicide
Other,
Father Deceased?
Yes
No
If Yes at what age?
≤ 29
30-39
40-49
50-59
60-69
70-79
80-89
≥ 90
Cause of Death Fathe
Heart Disease
Cancer
Stroke
Accident
Suicide
Other,

FIGURE 22A

ave you ever smoked? ☐ Yes ☐ No

yes, for how long? | | Years

0	0
1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9

[redacted] you been hospitalized past 5 years for more than 6 days at a time?
☐ Yes ☐ No

If y s, how many times?
☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9+

For each hospitalization (if not the same) how long did you stay and for what reason?

1) Weeks: ☐1 ☐2 ☐3 ☐4 ☐5 ☐6+
☐ Acute dis[redacted]ncluding infection and thrombosis
☐ Chronic Disorder
☐ Accident
☐ Other:

2) Weeks: ☐1 ☐2 ☐3 ☐4 ☐5 ☐6+
☐ Acute disorder, including infection and thrombosis
☐ Chronic Disorder
☐ Accident
☐ Other:

3) Weeks: ☐1 ☐2 ☐3 ☐4 ☐5 ☐6+
☐ Acute disorder, including infection and thrombosis
☐ Chronic Disorder
☐ Accident
☐ Other:

ave you r has anyone in your immediate family (parents, brothers, sisters, or your children) had the following?
lark all that apply!

Disease	You	Mother	Father	Sister	Brother	Child
Heart Disease, including arteriosclerosis	☐	☐	☐	☐	☐	☐
Stroke	☐	☐	☐	☐	☐	☐
Hypertension	☐	☐	☐	☐	☐	☐
Abdominal blood clots	☐	☐	☐	☐	☐	☐
Diabetes, insulin dependent	☐	☐	☐	☐	☐	☐
Diabetes, not insulin-dependent (diet controlled)	☐	☐	☐	☐	☐	☐
Cancer:	☐	☐	☐	☐	☐	☐
Lung & Bronchus	☐	☐	☐	☐	☐	☐
Breasts	☐	☐	☐	☐	☐	☐
Prostate	☐	☐	☐	☐	☐	☐
Colon & Rectum	☐	☐	☐	☐	☐	☐
Skin	☐	☐	☐	☐	☐	☐
Lymphoma & Leukemia	☐	☐	☐	☐	☐	☐
Other, please specify below:	☐	☐	☐	☐	☐	☐
☐						
Alzheimer's Disease	☐	☐	☐	☐	☐	☐
Epilepsy	☐	☐	☐	☐	☐	☐
Schizophrenia	☐	☐	☐	☐	☐	☐
☐						
Bipolar disorder (manic depression)	☐	☐	☐	☐	☐	☐
Major depression	☐	☐	☐	☐	☐	☐
Chronic Inflammatory or Autoimmune Disease including Multiple Sclerosis and Rheumatoid Arthritis	☐	☐	☐	☐	☐	☐
Emphysema	☐	☐	☐	☐	☐	☐
Asthma	☐	☐	☐	☐	☐	☐
Other, please specify below:	☐	☐	☐	☐	☐	☐
☐						

Do you take prescription drugs on a regular basis? ☐ Yes ☐ No

f yes, pleas specify below:

lave you ever donated blood before? Yes No

f yes, how many times: Number of Times

1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9

Additional health information details you would like to provide:

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[redacted]	6
2	7
3	8
4	9
5	0

Do you drink any kind of alcoholic beverage?

Never — Hardly ever
Less than 3 times per week — 3 or more times per week
Daily

FIGURE 22B

Collection Information

Consent Form Signed
☐ Yes ☐ N

Date of Collection
Month | Day | Year (2 0 0)
JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC

Time of Sample Collection (nearest hour, in 24 hour clock format)

Initials

Initials of Data Collector

(DO NOT COMPLETE; for data entry only)
Sample
☐ Intact
☐ Lost
☐ Broken
Volume (ml)

Bar Code

Donor Information

Date of Birth
Month | Year (1 9)
JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC

Sex:
☐ Male
☐ Female

Height
Ft. | Inches

Weight (lb)

What physical activity do you do on a regular basis?
☐ Running
☐ Swimming
☐ Biking
☐ Gymnastics
☐ Other
☐ None

Are you a vegetarian?
☐ Yes
☐ No

If Female:

How many times have you been pregnant?

How many times did you giv birth?

n which state lo you live?

To the best of your knowledge, what is the Ethnic Origin of your:

Father	Mother	
☐	☐	Caucasian (please mark specific geographic area below if known)
☐	☐	Northern Europe (Austria, Denmark, Finland, France, Germany, Netherlands, Norway, Sweden, Switzerland, UK)
☐	☐	Southern Europe (Greece, Italy, Spain, Turkey)
☐	☐	Eastern Europe (Czechoslovakia, Hungary, Poland, Russia, Yugoslavia)
☐	☐	Middle Eastern (Israel, Egypt, Iran, Iraq, Jordan, Syria, Other Arab States)
☐	☐	Other_____
☐	☐	Don't know

How long have you lived there? (Years)

How many years have you been smoking? (Years)

Did you quit smoking?
☐ Yes
☐ No

If yes, how many years ago? (Years)

How many cigarettes do/did you smoke per day? (Cigarettes)

Do you have Lung Emphysema?
☐ Yes
☐ No

If yes, for how long? (Years)

Continue on back →

FIGURE 22C

...u completed in school?
- less than 8th grade
- 8th, 9th, 10th, or 11th grade
- high school graduate or equivalency
- some college, 2 yr degree
- college graduate, 4 yr degree
- post graduate education or degree

[redacted]
- Y 6
- No

If Yes at what age?
- ≤ 29
- 30-39
- 40-49
- 50-59
- 60-69
- 70-79
- 80-89
- ≥ 90

[redacted]
- Heart Disease
- Cancer
- Stroke
- Accident
- Suicide
- Other,_____

[redacted]
- Yes
- No

If Yes at what age?
- ≤ 29
- 30-39
- 40-49
- 50-59
- 60-69
- 70-79
- 80-89
- ≥ 90

[redacted]
- Heart Disease
- Cancer
- Stroke
- Accident
- Suicide
- Other,_____

ealth Information

ive you or has anyone in your immediate family (parents, brothers, sisters, or your children) had the following?
ark all that apply!

Disease	You	Mother	Father	Sister	Brother	Child
eart Disease	☐	☐	☐	☐	☐	☐
troke	☐	☐	☐	☐	☐	☐
ypertension	☐	☐	☐	☐	☐	☐
bdominal blood clots	☐	☐	☐	☐	☐	☐
iabetes, insulin dependent	☐	☐	☐	☐	☐	☐
iabetes, not insulin-dependent (diet controlled)	☐	☐	☐	☐	☐	☐
ancer:	☐	☐	☐	☐	☐	☐
Lung & Bronchus	☐	☐	☐	☐	☐	☐
Breasts	☐	☐	☐	☐	☐	☐
Prostate	☐	☐	☐	☐	☐	☐
C lon & Rectum	☐	☐	☐	☐	☐	☐
Skin	☐	☐	☐	☐	☐	☐
Lymphoma & Leukemia	☐	☐	☐	☐	☐	☐
Other, please specify below:	☐	☐	☐	☐	☐	☐
☐						
lzheimer's Disease	☐	☐	☐	☐	☐	☐
pilepsy	☐	☐	☐	☐	☐	☐
chizophrenia	☐	☐	☐	☐	☐	☐
ipolar disorder (manic depression)	☐	☐	☐	☐	☐	☐
lajor depression	☐	☐	☐	☐	☐	☐
hronic Inflammatory or Autoimmune Disease including Multiple Sclerosis and Rheumatoid Arthritis	☐	☐	☐	☐	☐	☐
☐						
mphysema	☐	☐	☐	☐	☐	☐
sthma	☐	☐	☐	☐	☐	☐
ther, please specify below:	☐	☐	☐	☐	☐	☐

o you take prescription drugs on a regular basis? ☐ Yes ☐ No

f yes, please specify below:

Have you ever donated blood before? ☐ Yes ☐ No

If yes, how many times: Number of Times

lav you been hospitalized 1 the past 5 years for more han 6 days at a time?
☐ Yes ☐ No

f yes, how many times?

or each hospitalization if not the same) ow long did you stay nd for what reason?

1) Weeks: [redacted]
- ☐ Acute disorder, including infection and thrombosis
- ☐ Chronic Disorder
- ☐ Accident
- ☐ Other:_____

2) Weeks: [redacted]
- ☐ Acute disorder, including infection and thrombosis
- ☐ Chronic Disorder
- ☐ Accident
- ☐ Other:_____

3) Weeks: [redacted]
- ☐ Acute disorder, including infection and thrombosis
- ☐ Chronic Disorder
- ☐ Accident
- ☐ Other:_____

Do you drink any kind of alcoholic beverage?
- ☐ Never
- ☐ Hardly ever
- ☐ Less than 3 times per week
- ☐ 3 or more times per week
- ☐ Daily

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dditional health information details you would like to provide:

_____

_____

FIGURE 22D

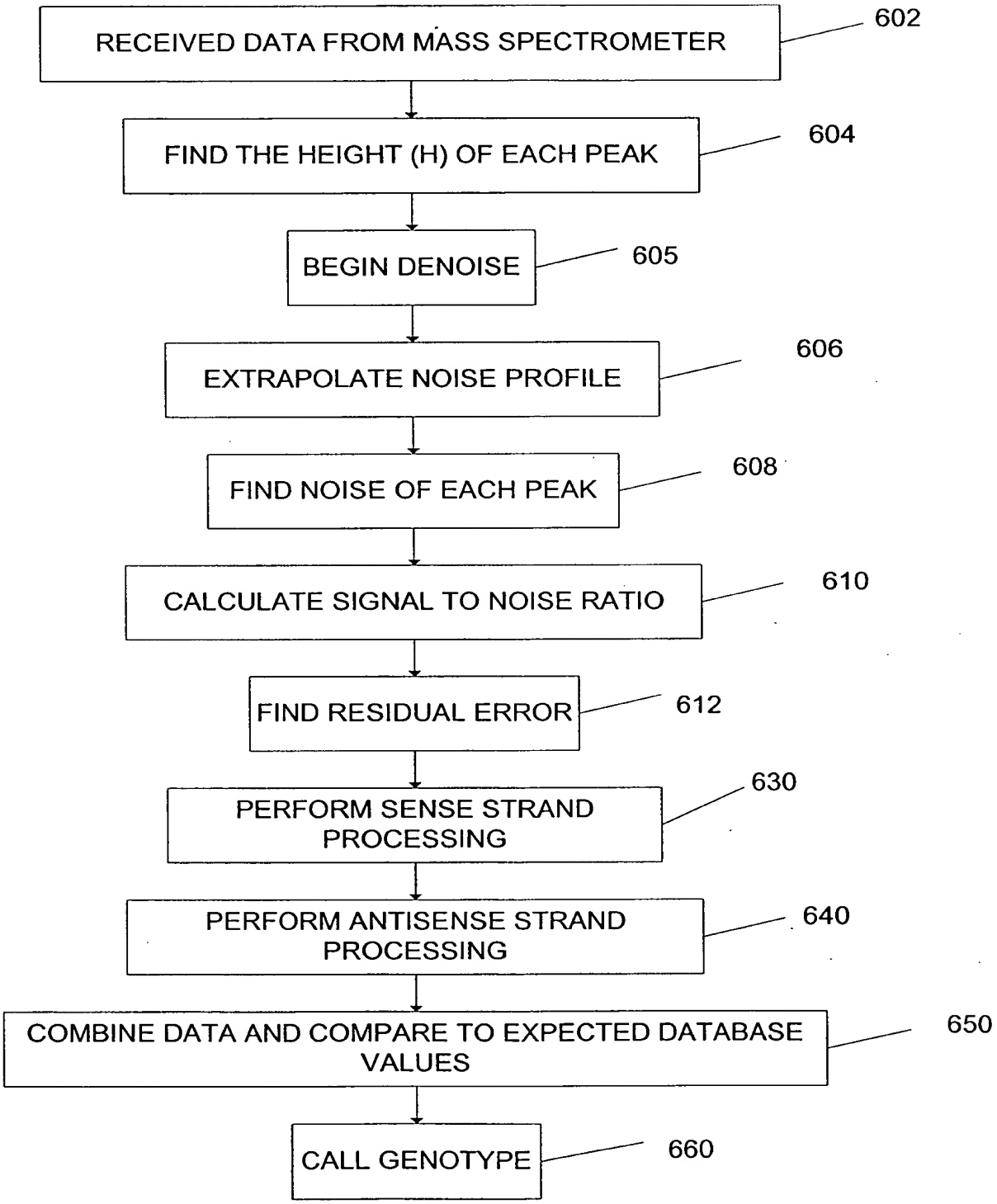

RECEIVED DATA FROM MASS SPECTROMETER
602
FIND THE HEIGHT (H) OF EACH PEAK
604
BEGIN DENOISE
605
EXTRAPOLATE NOISE PROFILE
606
FIND NOISE OF EACH PEAK
608
CALCULATE SIGNAL TO NOISE RATIO
610
FIND RESIDUAL ERROR
612
PERFORM SENSE STRAND PROCESSING
630
PERFORM ANTISENSE STRAND PROCESSING
640
COMBINE DATA AND COMPARE TO EXPECTED DATABASE VALUES
650
CALL GENOTYPE
660

FIGURE 23

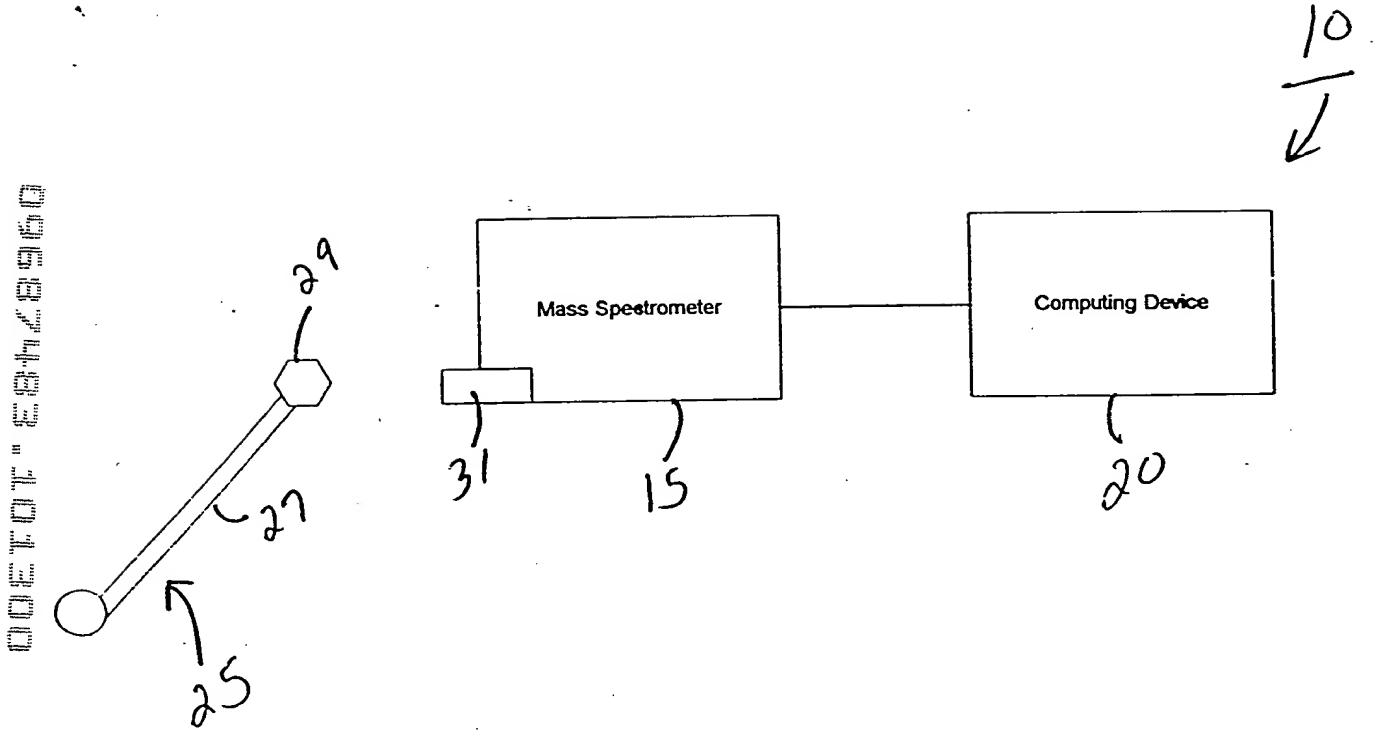


FIGURE 24

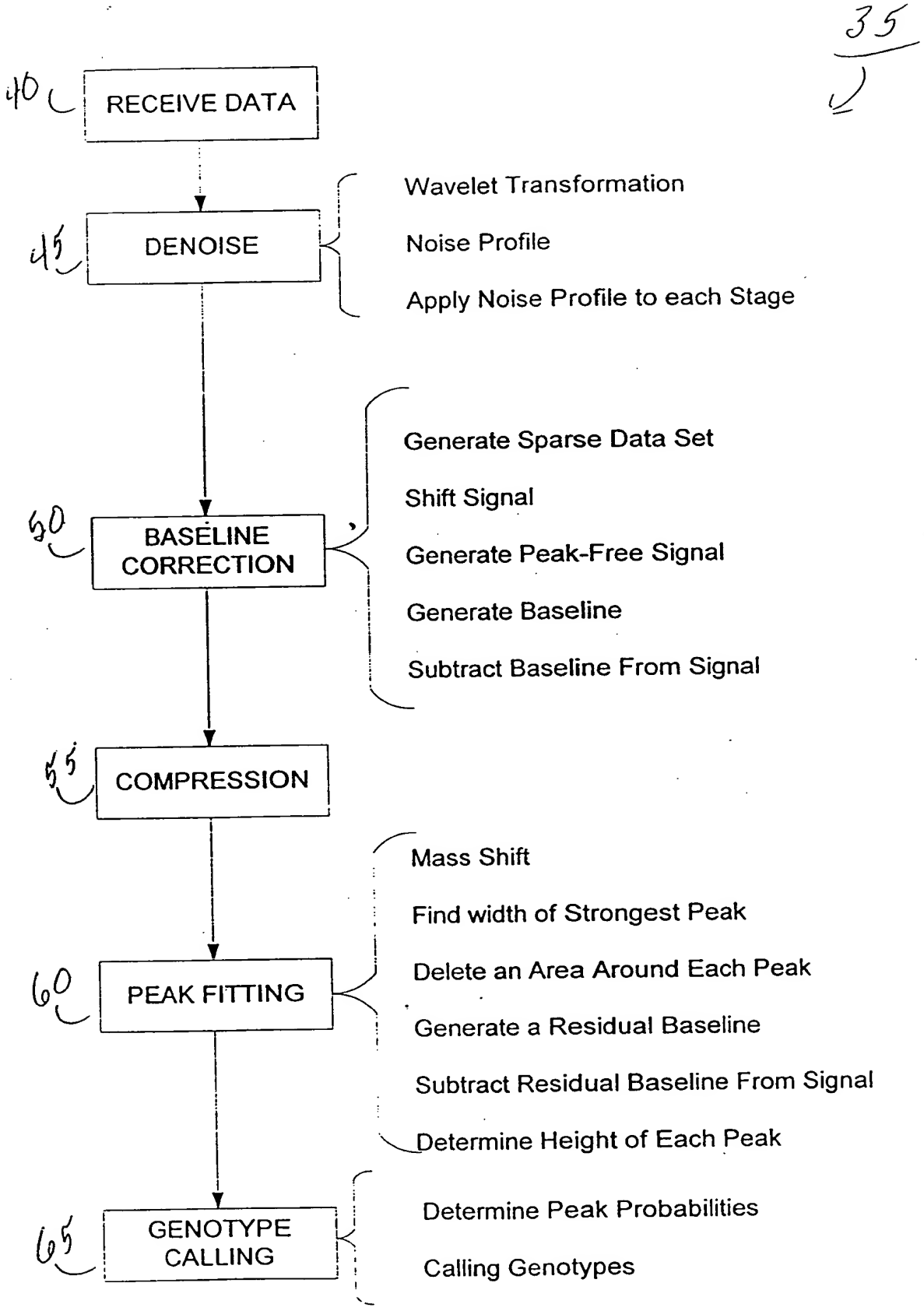

35
40
RECEIVE DATA
45
DENOISE
Wavelet Transformation
Noise Profile
Apply Noise Profile to each Stage
50
BASELINE CORRECTION
Generate Sparse Data Set
Shift Signal
Generate Peak-Free Signal
Generate Baseline
Subtract Baseline From Signal
55
COMPRESSION
60
PEAK FITTING
Mass Shift
Find width of Strongest Peak
Delete an Area Around Each Peak
Generate a Residual Baseline
Subtract Residual Baseline From Signal
Determine Height of Each Peak
65
GENOTYPE CALLING
Determine Peak Probabilities
Calling Genotypes

FIGURE 25

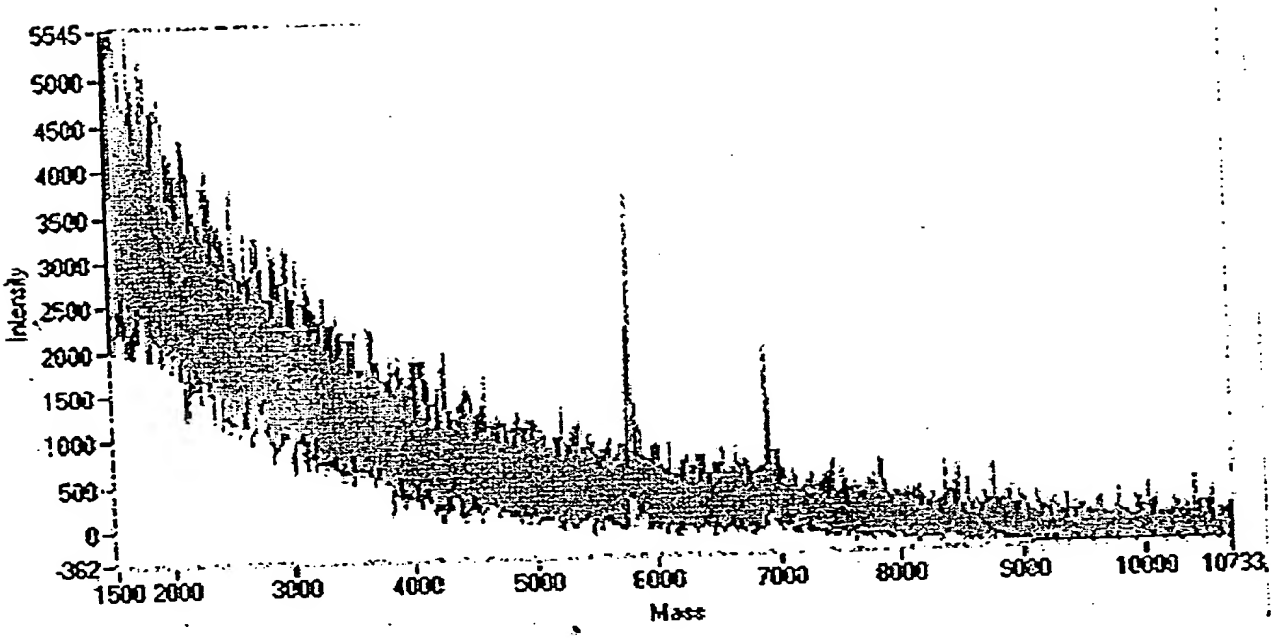


FIGURE 26

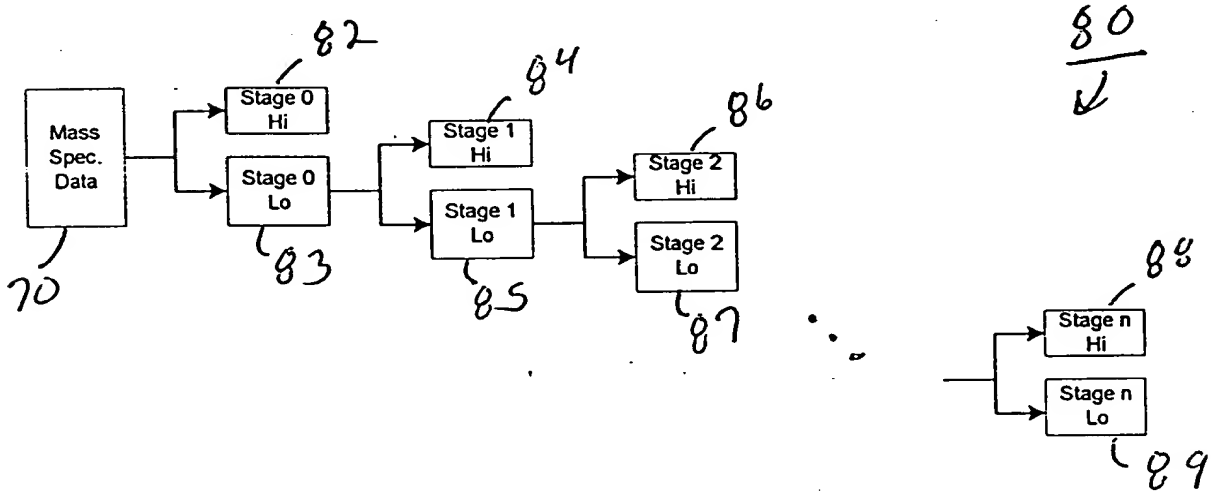


FIGURE 27

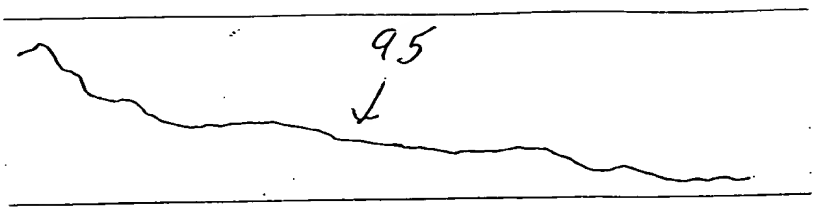
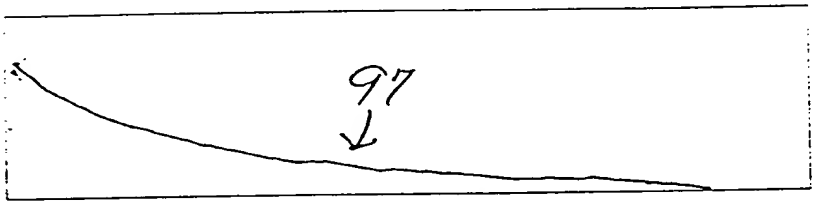


FIGURE 28



Exp fitting
$a_0 + a_1 \exp^{-}(a_2 m)$

FIGURE 29

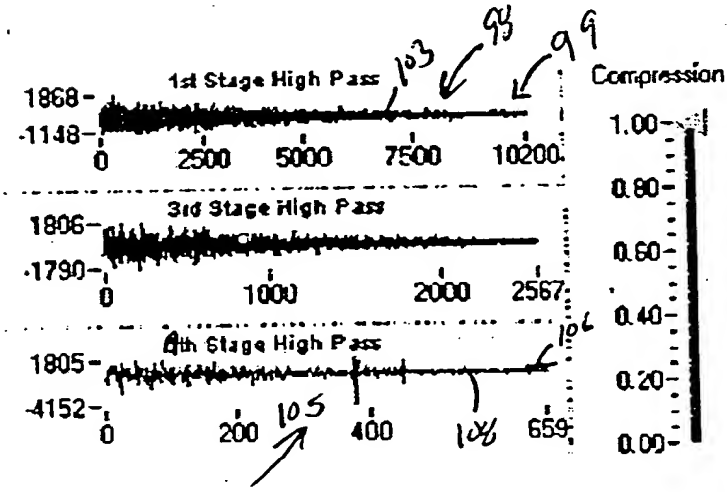
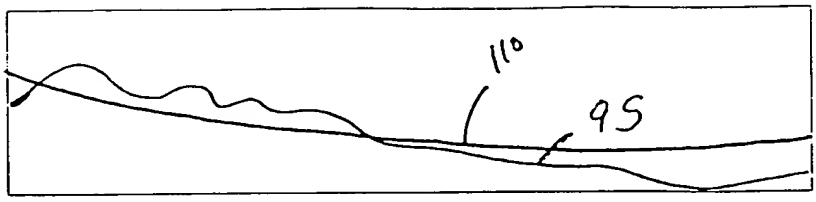


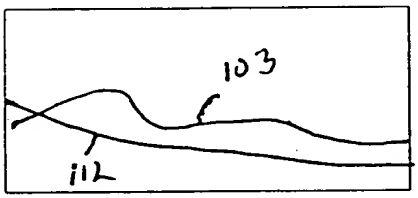
FIGURE 30

09374808.1

Stage 0 - Hi

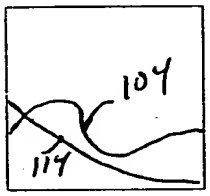


Threshold 0=4XNoiseProfile



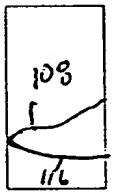
Stage 1 - Hi

Threshold 1=2XNoiseProfile



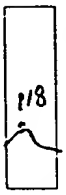
Stage 2 - Hi

Threshold 2=1XNoiseProfile



Stage n - Hi

Threshold n=(1/2^{n-2})XNoiseProfile



Stage n - Lo

FIGURE 31

DOCKET ALARM

120

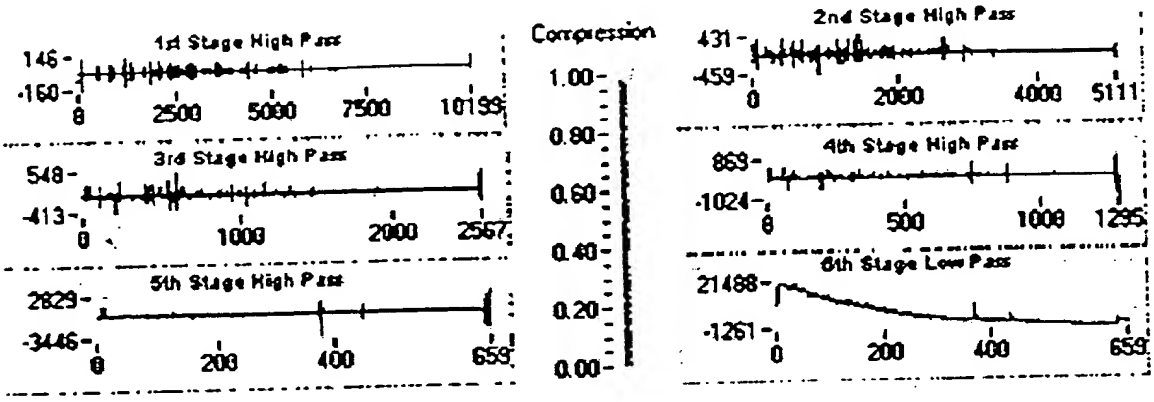
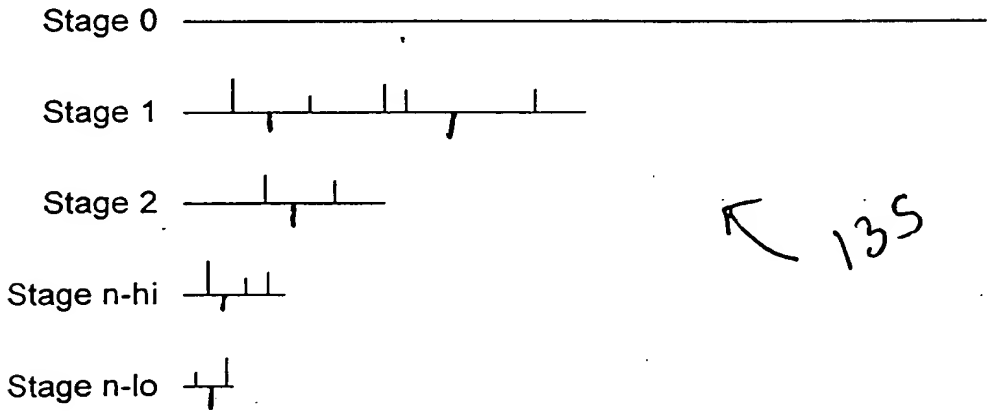


FIGURE 32

Signal (t)= $\frac{(\text{Start } 0(t) + \text{Start } 1(t) + \text{Start } 2(t) \ldots + \text{Start } 23(t))}{24}$

FIGURE 33 SHIFT SIGNAL TO ACCOUNT FOR VARIATIONS DUE TO STARTING POINT



135

FIGURE 34

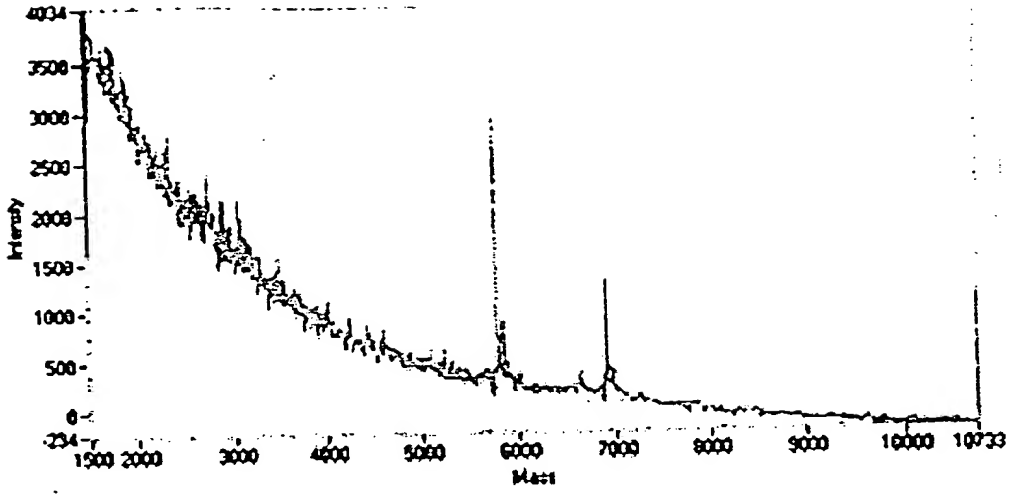


FIGURE 35

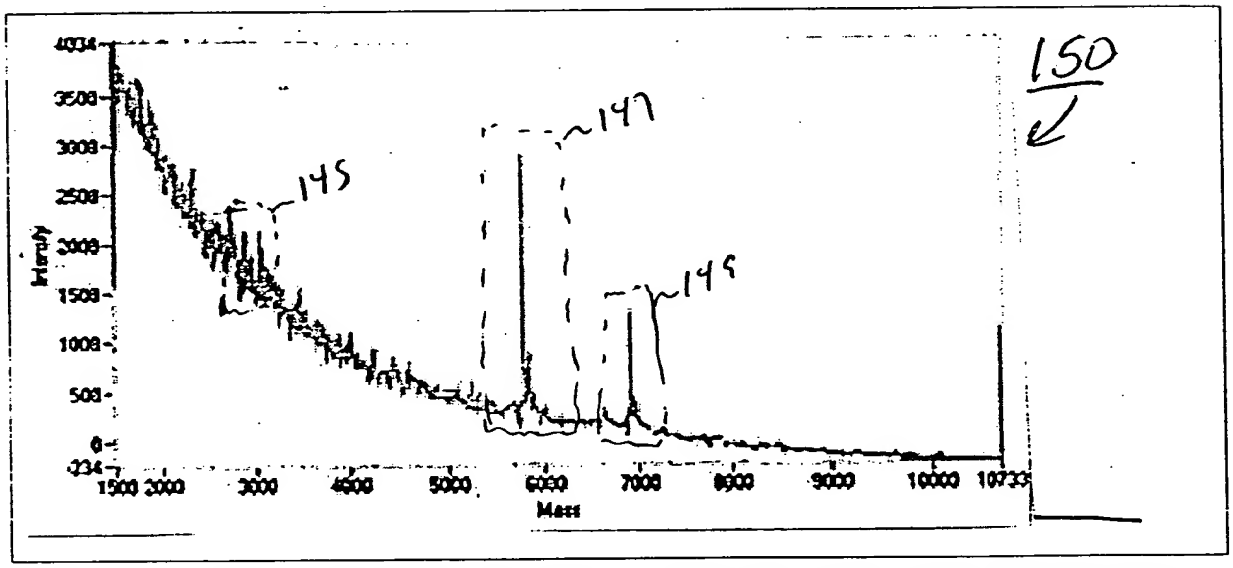


FIG. 13 - TAKE A MOVING AVERAGE, REMOVE SECTIONS EXCEDING A THRESHOLD

FIGURE 36

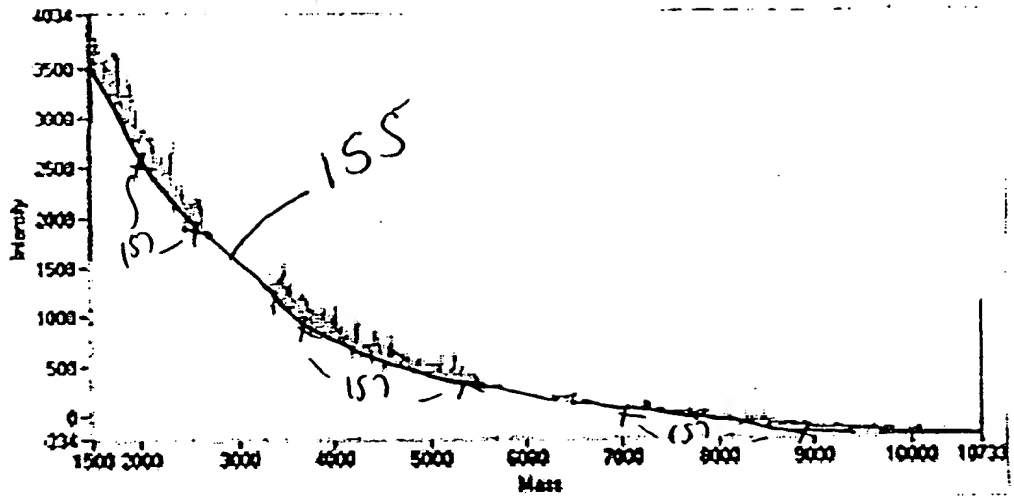
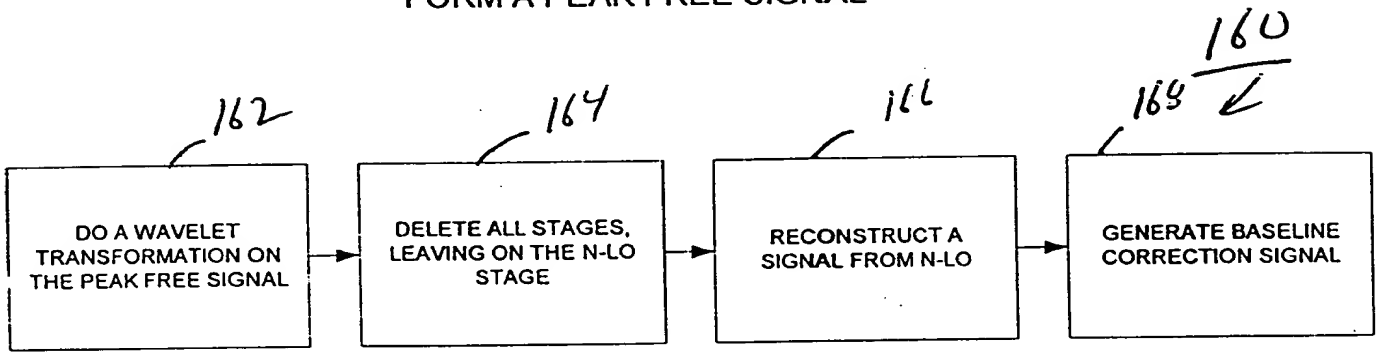


FIGURE 37

FIND MINIMA IN REMAINING SIGNALS AND CONNECT TO FORM A PEAK FREE SIGNAL



GENERATE BASELINE CORRECTION

FIGURE 38

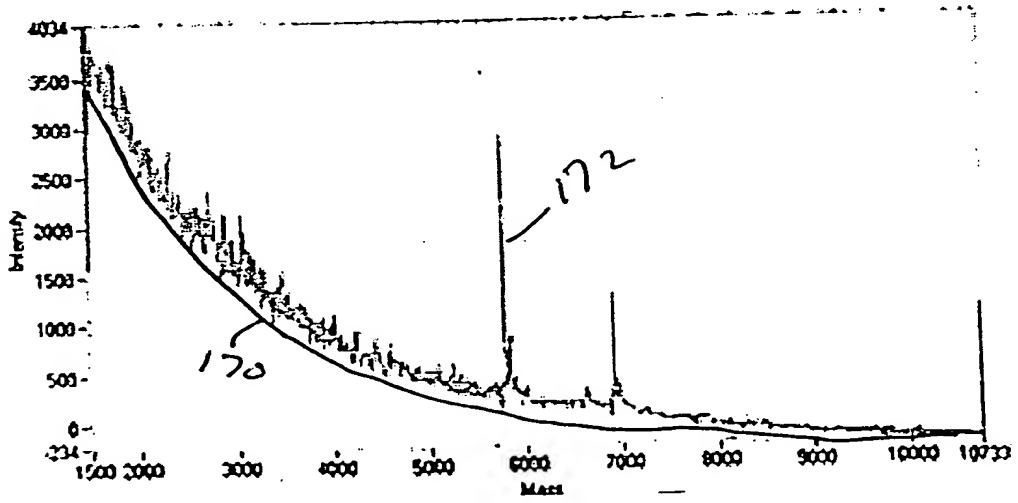


FIGURE 39

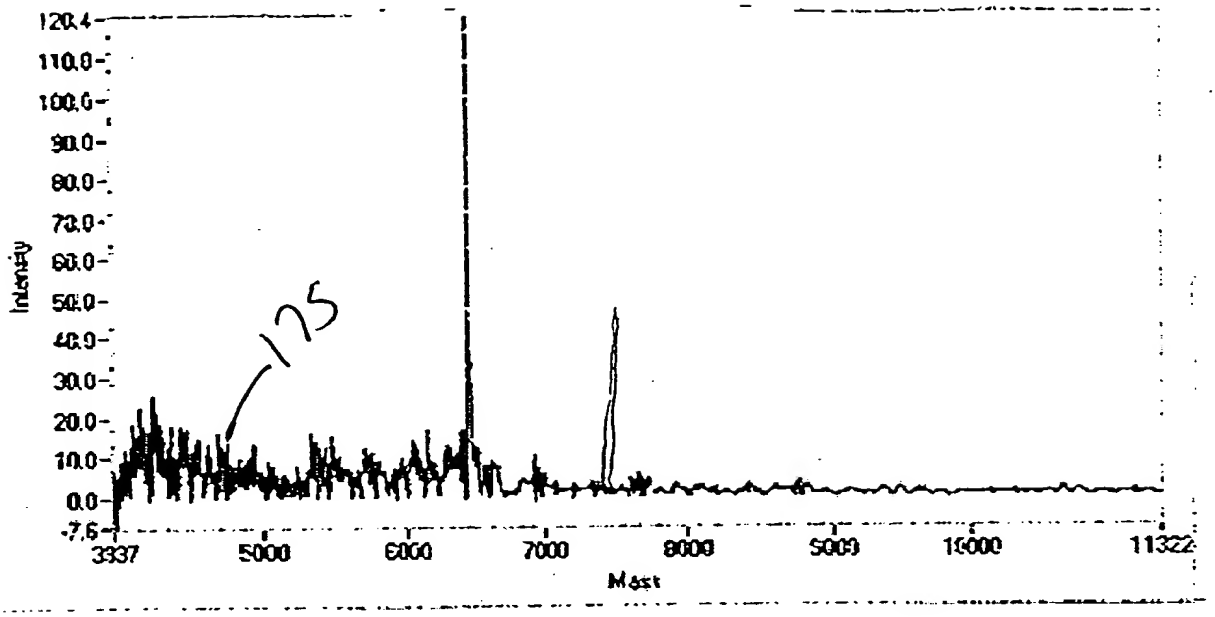


FIGURE 40

NON-0 COEFFICIENTS	VALUE	INTERMEDIATE	RELATIVE
100	25	100.025	100.025
150	220	150.220	50.220
500	.1	500.0001	350.0001
10,050	800	10,050.8	9550.8
10,075	890	10,075.89	25.89
11,125	910	11,125.91	150.91
12,100	1000 (MAX)	12,100.99999	975.99999
13,250	940	13,250.94	1150.94

FIGURE 41

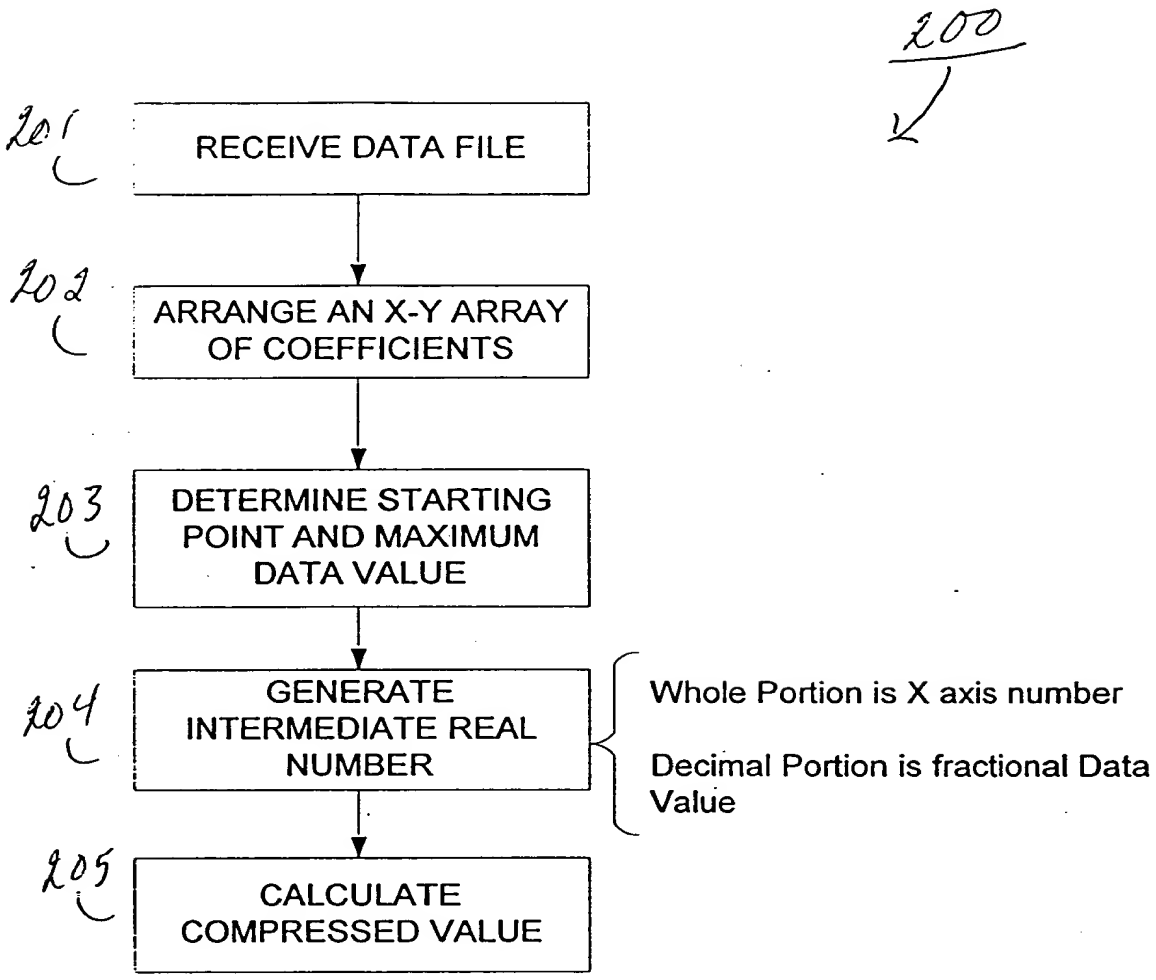

200
201
RECEIVE DATA FILE
202
ARRANGE AN X-Y ARRAY OF COEFFICIENTS
203
DETERMINE STARTING POINT AND MAXIMUM DATA VALUE
204
GENERATE INTERMEDIATE REAL NUMBER
Whole Portion is X axis number
Decimal Portion is fractional Data Value
205
CALCULATE COMPRESSED VALUE

FIGURE 42

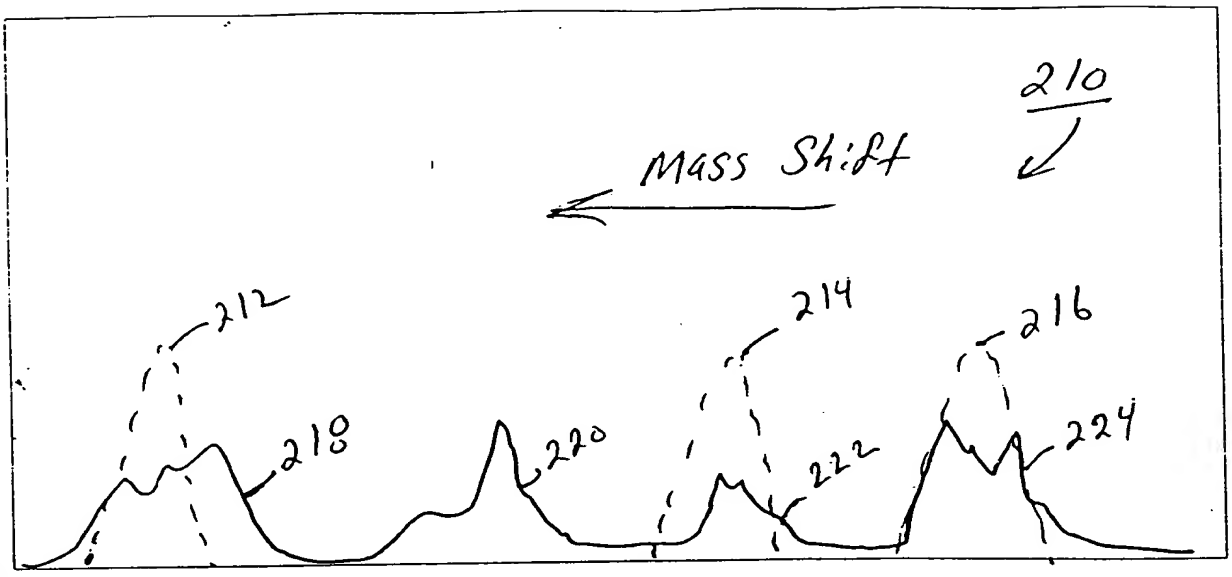


FIGURE 43

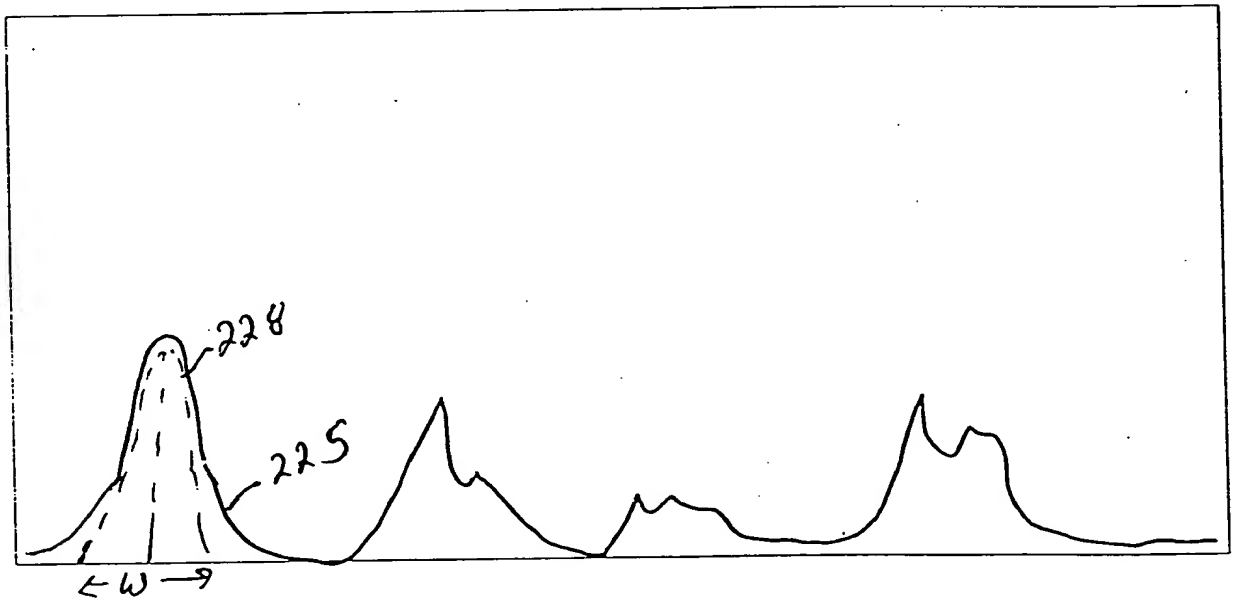


FIGURE 44

Doc Code: IDS.03082008

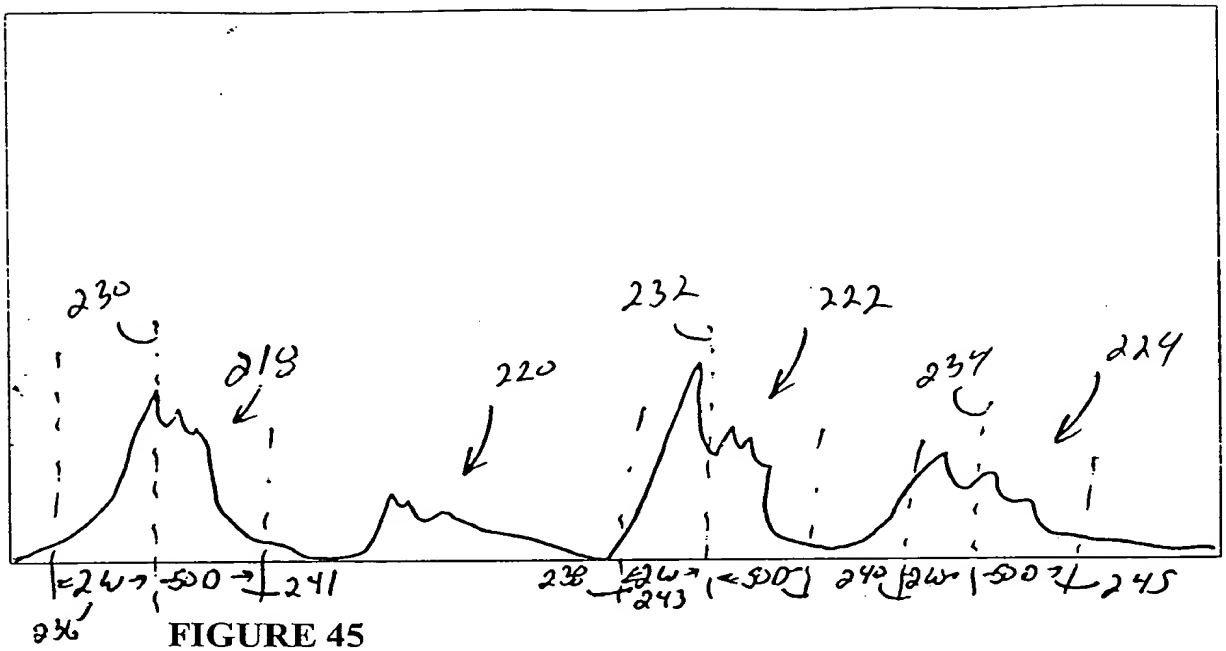


FIGURE 45

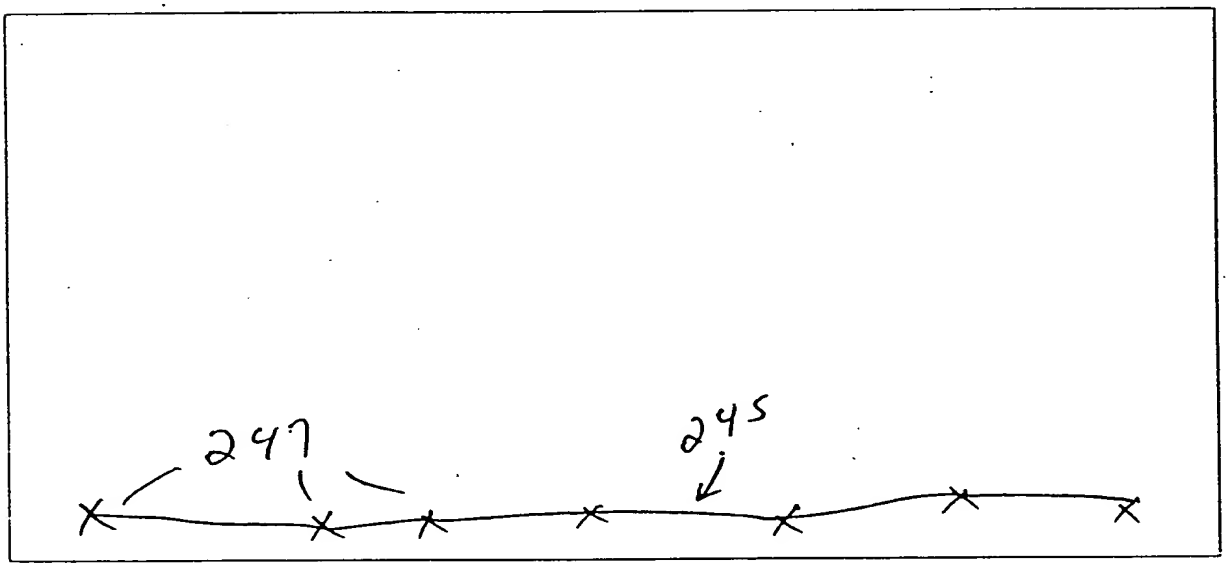


FIGURE 46

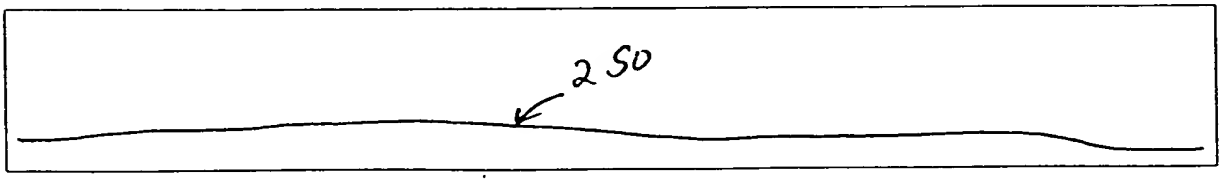


FIGURE 47

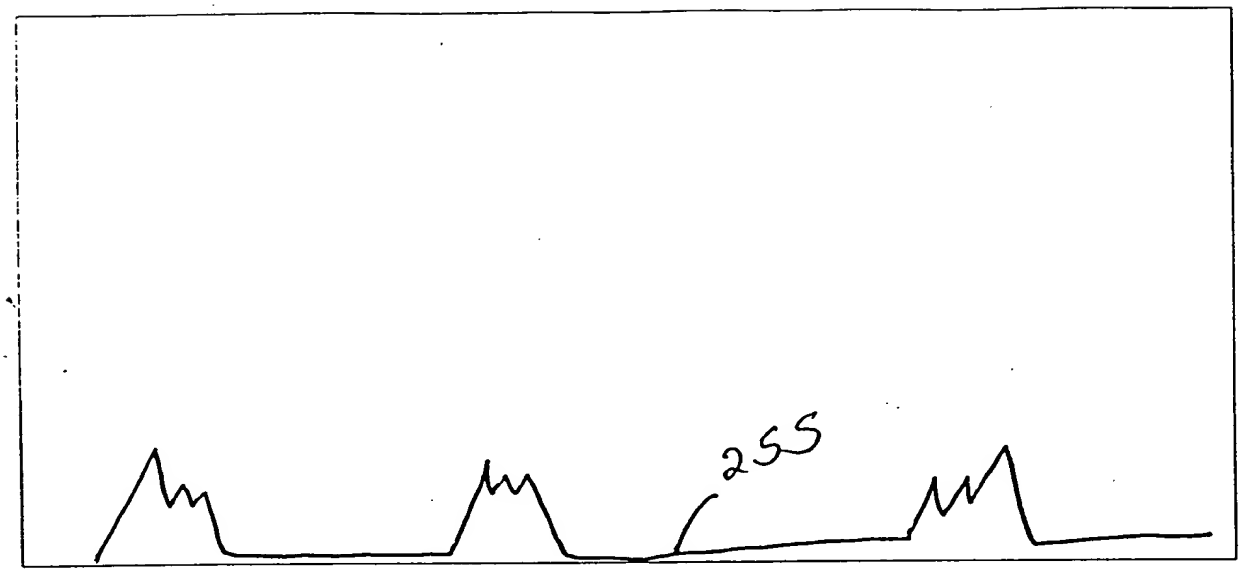


FIGURE 48

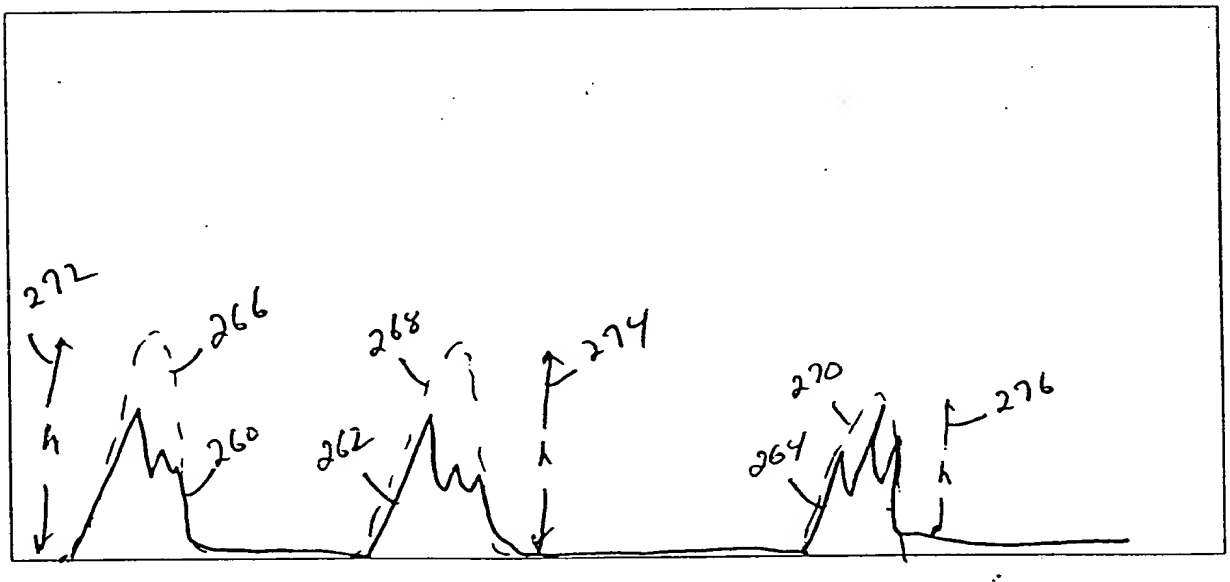


FIGURE 49

0068748.0003

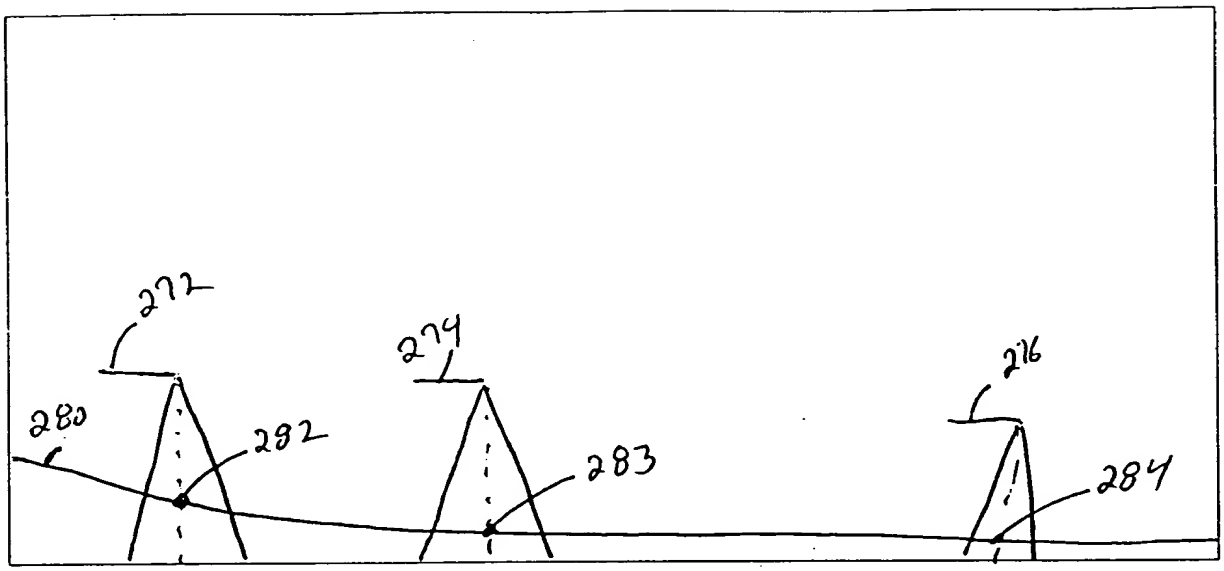


FIGURE 50

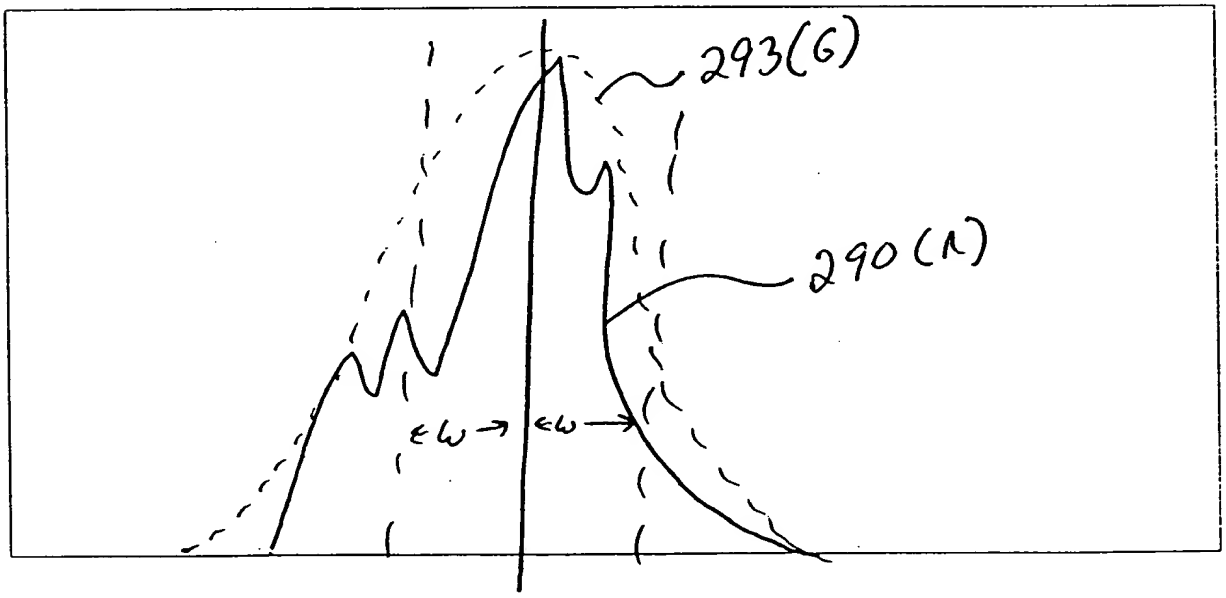


FIGURE 51

0060-1003-0056

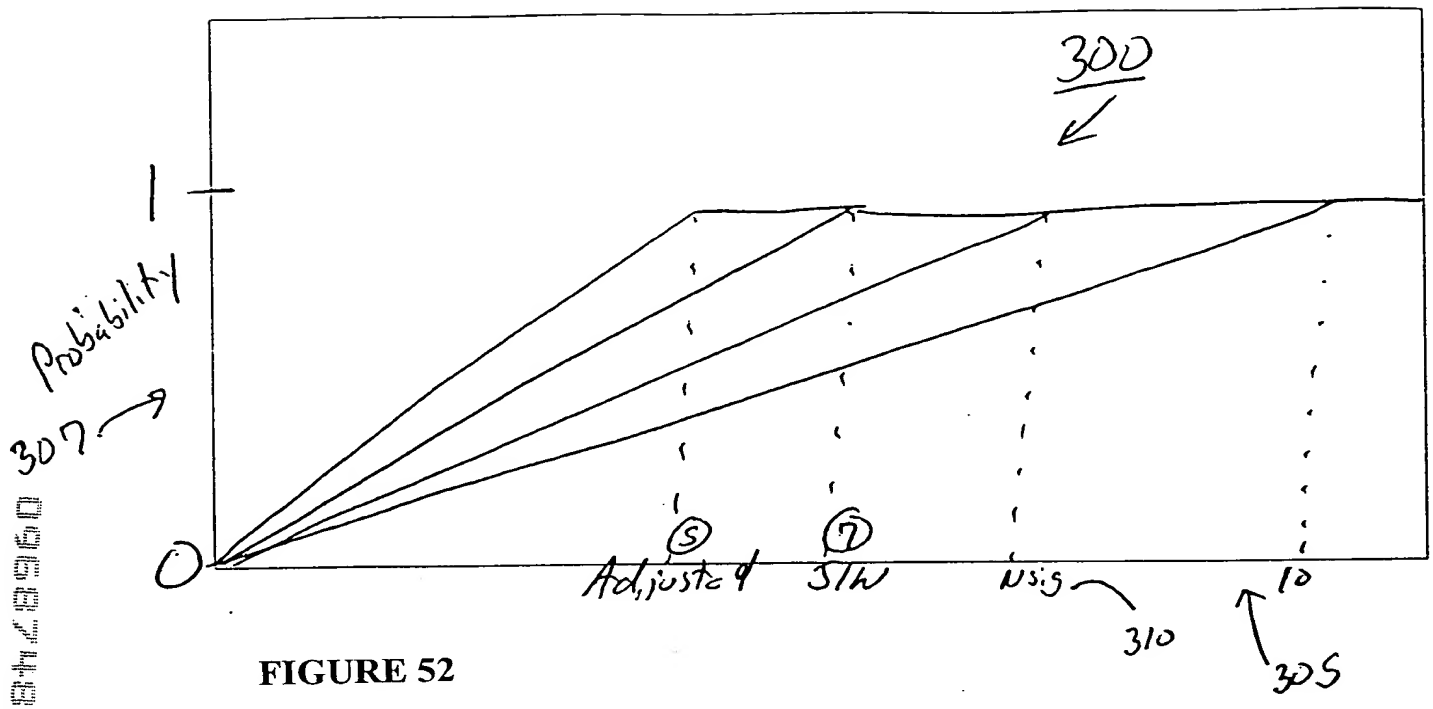


FIGURE 52

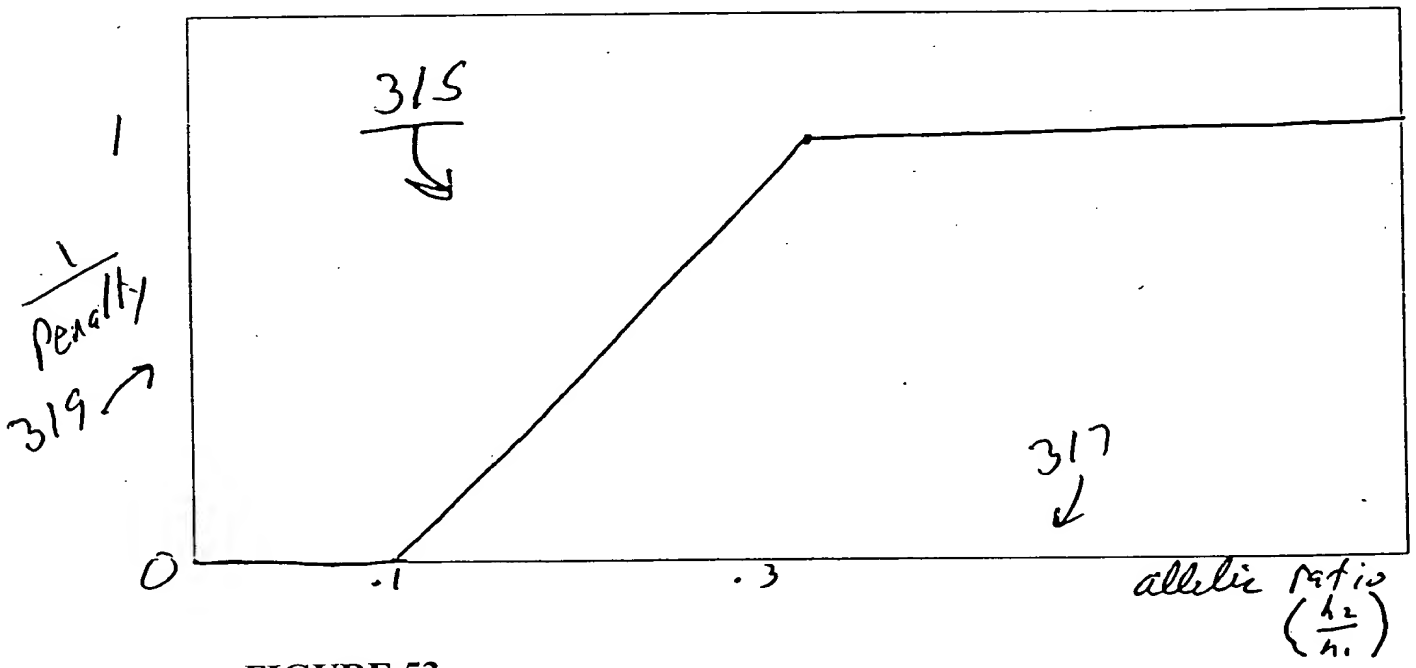
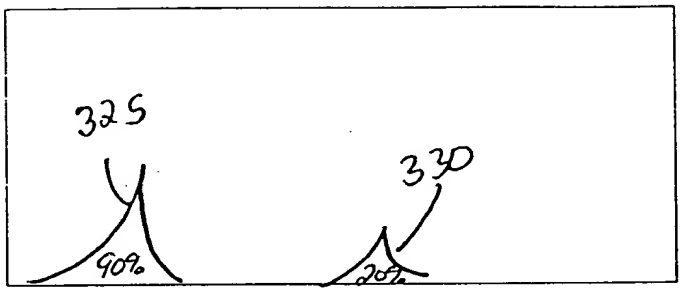


FIGURE 53



329
PROBABILITY OF GG EXISTING:
P(GG) = P(G) * P(1-C)
=90% * (100% - 20%)
=90% * 80%
=72%

331
PROBABILITY OF CC EXISTING:
P(CC) = P(C) * P(1-G)
=20% * (100% - 90%)
=20% * 10%
= 2%

333
PROBABILITY OF GC EXISTING:
P(GC) = P(G) * P(C)
=90% *20%
=18%

FIGURE 54

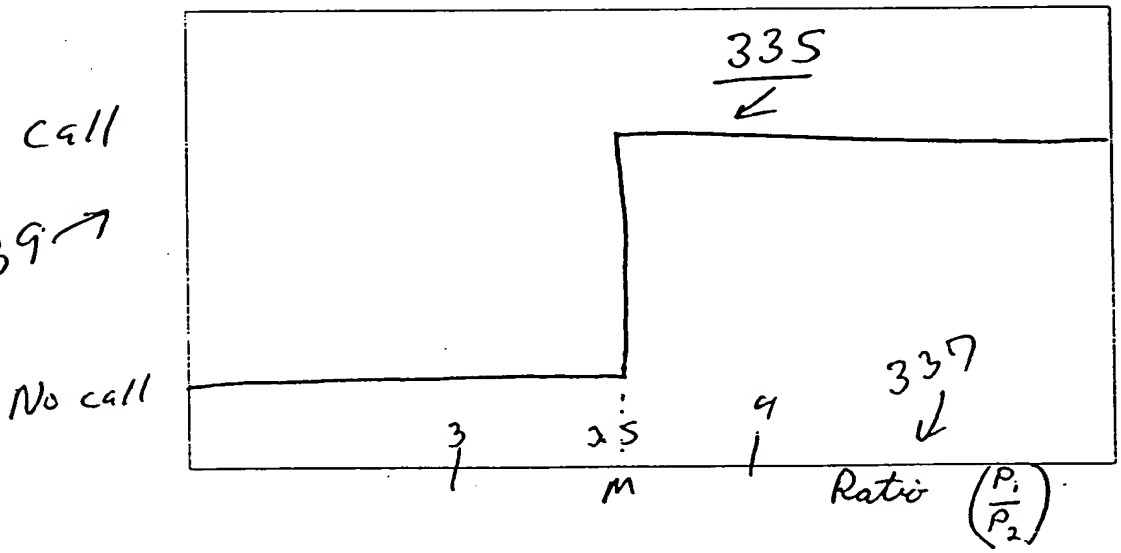


FIGURE 55

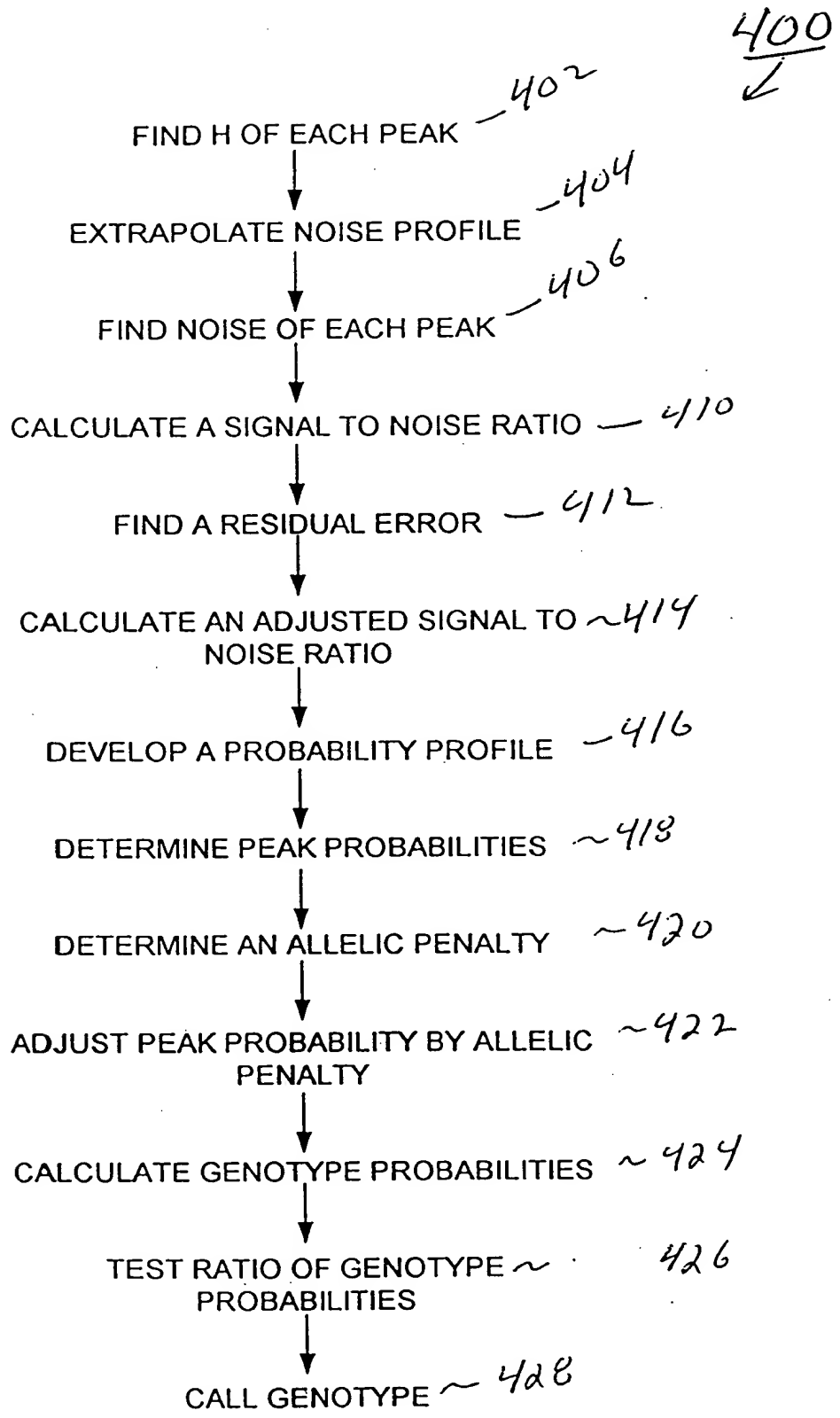

400
FIND H OF EACH PEAK
402
EXTRAPOLATE NOISE PROFILE
404
FIND NOISE OF EACH PEAK
406
CALCULATE A SIGNAL TO NOISE RATIO
410
FIND A RESIDUAL ERROR
412
CALCULATE AN ADJUSTED SIGNAL TO NOISE RATIO
414
DEVELOP A PROBABILITY PROFILE
416
DETERMINE PEAK PROBABILITIES
418
DETERMINE AN ALLELIC PENALTY
420
ADJUST PEAK PROBABILITY BY ALLELIC PENALTY
422
CALCULATE GENOTYPE PROBABILITIES
424
TEST RATIO OF GENOTYPE PROBABILITIES
426
CALL GENOTYPE
428

FIGURE 56

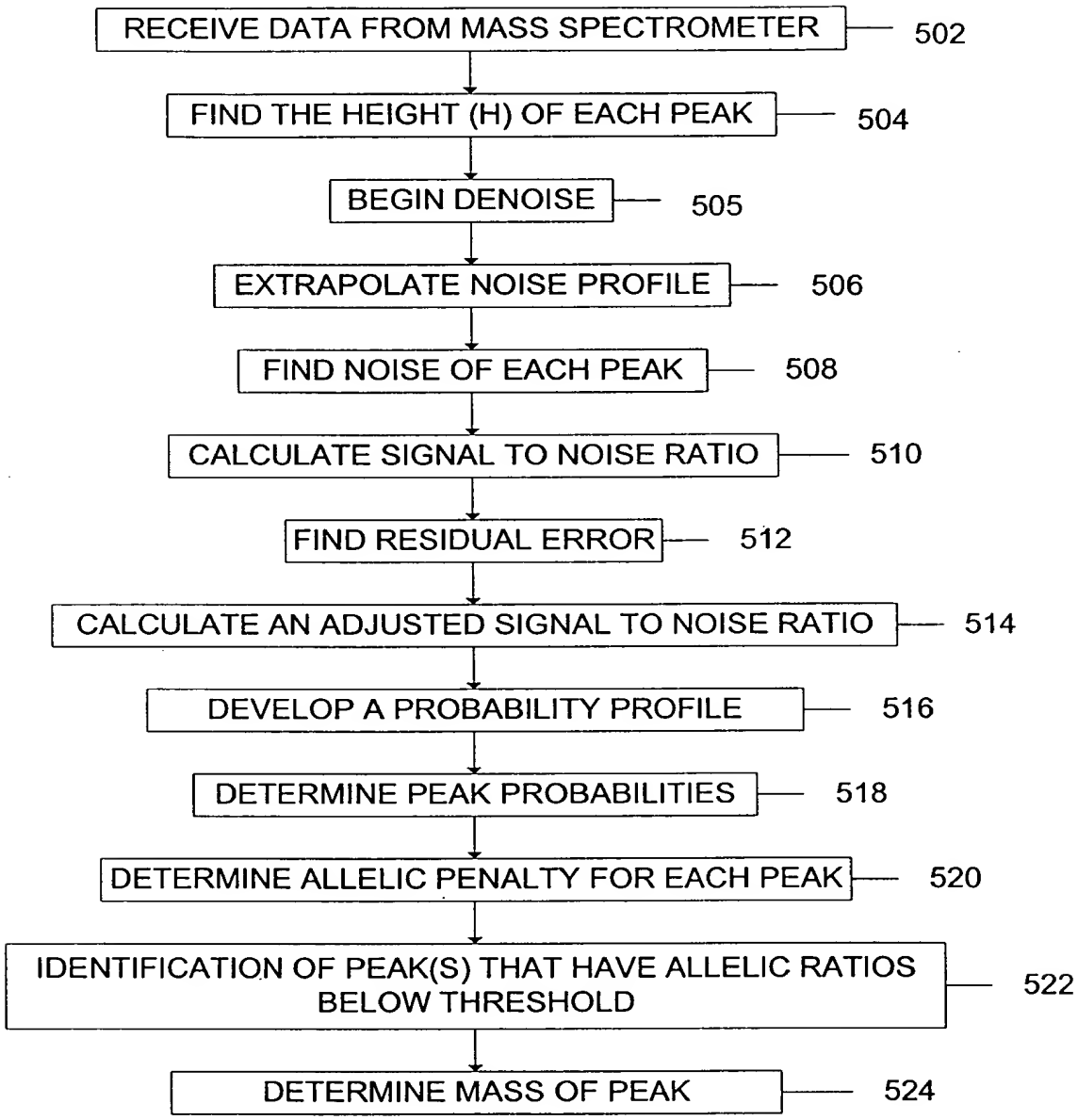

RECEIVE DATA FROM MASS SPECTROMETER
502
FIND THE HEIGHT (H) OF EACH PEAK
504
BEGIN DENOISE
505
EXTRAPOLATE NOISE PROFILE
506
FIND NOISE OF EACH PEAK
508
CALCULATE SIGNAL TO NOISE RATIO
510
FIND RESIDUAL ERROR
512
CALCULATE AN ADJUSTED SIGNAL TO NOISE RATIO
514
DEVELOP A PROBABILITY PROFILE
516
DETERMINE PEAK PROBABILITIES
518
DETERMINE ALLELIC PENALTY FOR EACH PEAK
520
IDENTIFICATION OF PEAK(S) THAT HAVE ALLELIC RATIOS BELOW THRESHOLD
522
DETERMINE MASS OF PEAK
524

FIGURE 57

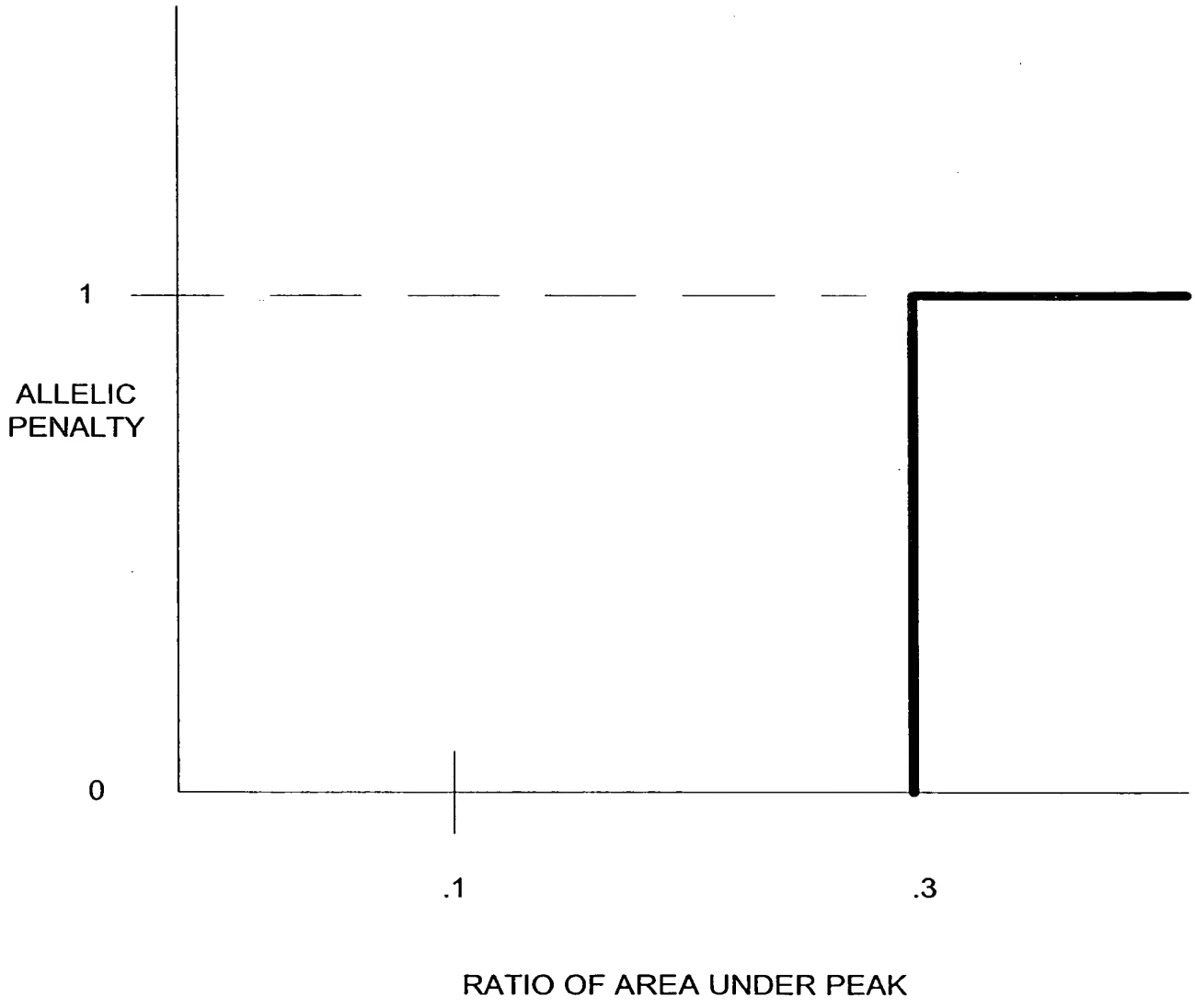


FIGURE 58